# Synovial Metaplasia, A Specialized Form of Repair

## A Case Report and Review of the Literature

*Marjorie R. Fowler, MD; Cherie-Ann O. Nathan, MD; Fleurette Abreo, MD*

**• Synovial metaplasia is a change seen most frequently in the tissues surrounding silicone breast prostheses and in healing tissue adjacent to joint prostheses. It has also been described in skin and soft tissues, most frequently in healing or healed traumatic or surgical wounds. We report a case of synovial metaplasia occurring in a hitherto unreported location, namely, adjacent to a silicone low-pressure voice prosthesis. A review of cases of synovial metaplasia reported in the literature revealed that in most cases, spaces that form adjacent to foreign material (most commonly silicone breast prostheses) and the smooth gliding surfaces of the foreign material that resist penetration by fibroblast processes are frequent associated findings that precede the occurrence of synovial metaplasia. Thus, synovial metaplasia might represent a specialized form of healing in cases that have this combination of physical features.**

**(*Arch Pathol Lab Med.* 2002;126:727–730)**

Synovial hyperplasia and giant cell reaction in response to intact and fragmented plastic prosthetic joints have been well known for many years.[1] Goldring et al[2] demonstrated that the membranes that formed away from the joint cavity adjacent to the methacrylate cement used to hold hip prostheses were similar to true joint synovial membranes in the same patients. Like native synovium, the new membranes contained epithelioid cells that were oriented so that the cell bodies were perpendicular to the methacrylate surface. These membranes were occasionally thrown into papillary folds. Histochemical staining, cell cultures, and organ cultures failed to reveal any differences in the membranes adjacent to the methacrylate cement and the native joint synovial membranes of these individuals. The organ cultures of the new membranes even released prostaglandin $E_2$ and collagenase into the media, like regenerating synovium. Studies by Hunter et al[3] showed that the same type of membranes would form around the gliding surfaces of silastic rods used in staged tendon repair.

More recently, the formation of synovial-like tissue in response to another type of prosthetic device, the silicone breast implant and expander, has been described extensively.[4–9] This tissue is located well away from joint spaces and broadened the circumstances under which one would expect to see synovial metaplasia. In addition to breast silicone prostheses, we found 1 reported case of synovial metaplasia occurring around a testicular implant.[4] Synovial metaplasia has been described most frequently in association with the textured type of silicone breast prosthesis. A morphologic variant of synovial metaplasia also most frequently seen with the textured implants is the papillary type.

We report the first case, to our knowledge, in which papillary synovial metaplasia has occurred secondary to long-term placement of a silicone voice prosthesis.

### REPORT OF A CASE

A 57-year-old woman presented to the Otolaryngology Clinic in May 1996 with a 2-month history of increasing hoarseness and sore throat. Following panendoscopy and biopsy, a diagnosis of squamous cell carcinoma of the larynx was rendered, for which she underwent a total laryngectomy with a left modified radical neck dissection and a right selective neck dissection with a tracheal stoma. Her past history was significant for smoking, drinking alcohol, and a hysterectomy. Four months after the resection, she underwent a tracheoesophageal puncture with placement of a silicone 2.6-mm low-pressure Blom-Singer Voice Prosthesis (In Health Technologies, Carpinteria, Calif). This device has an esophageal 1-way valve that protects the airway during swallowing and opens under positive tracheal pressure so that air passes into the esophagus. This allows the patient to produce the sounds necessary for the production of esophageal speech. The prosthesis is fixed to the skin overlying the stoma with a silicone safety strap. The stomal size was evaluated at regular follow-up visits to the Otolaryngology Clinic. The stomal size was stable and without granulation tissue or other obstructing or stenosing lesions until the follow-up visit of November 2000. At that time, a peristomal lesion clinically felt to be granulation tissue was noted and a biopsy was performed.

### MATERIALS AND METHODS

The tissue was fixed in 10% neutral phosphate-buffered formalin and embedded in paraffin for routine histology. Immunohistochemistry was performed using the streptavidin-biotin complex method using antibodies directed against the following antigens: pan-keratin, CD68, S100, and vimentin (Ventana Medical Systems Inc, Tucson, Ariz) using a Ventana Nexus IHC automated immunostainer.

### PATHOLOGIC FINDINGS

Histologic examination of the biopsy tissue revealed skin overlying a fistulous space with a papillary surface

Accepted for publication October 8, 2001.

From the Departments of Pathology (Drs Fowler and Abreo) and Otolaryngology (Dr Nathan), Louisiana State University Health Sciences Center, Shreveport.

Reprints: Marjorie R. Fowler, MD, Department of Pathology, Louisiana State University Health Sciences Center, Shreveport, PO Box 33932, Shreveport, LA 71130-3932 (e-mail: Mfowle@lsuhsc.edu).

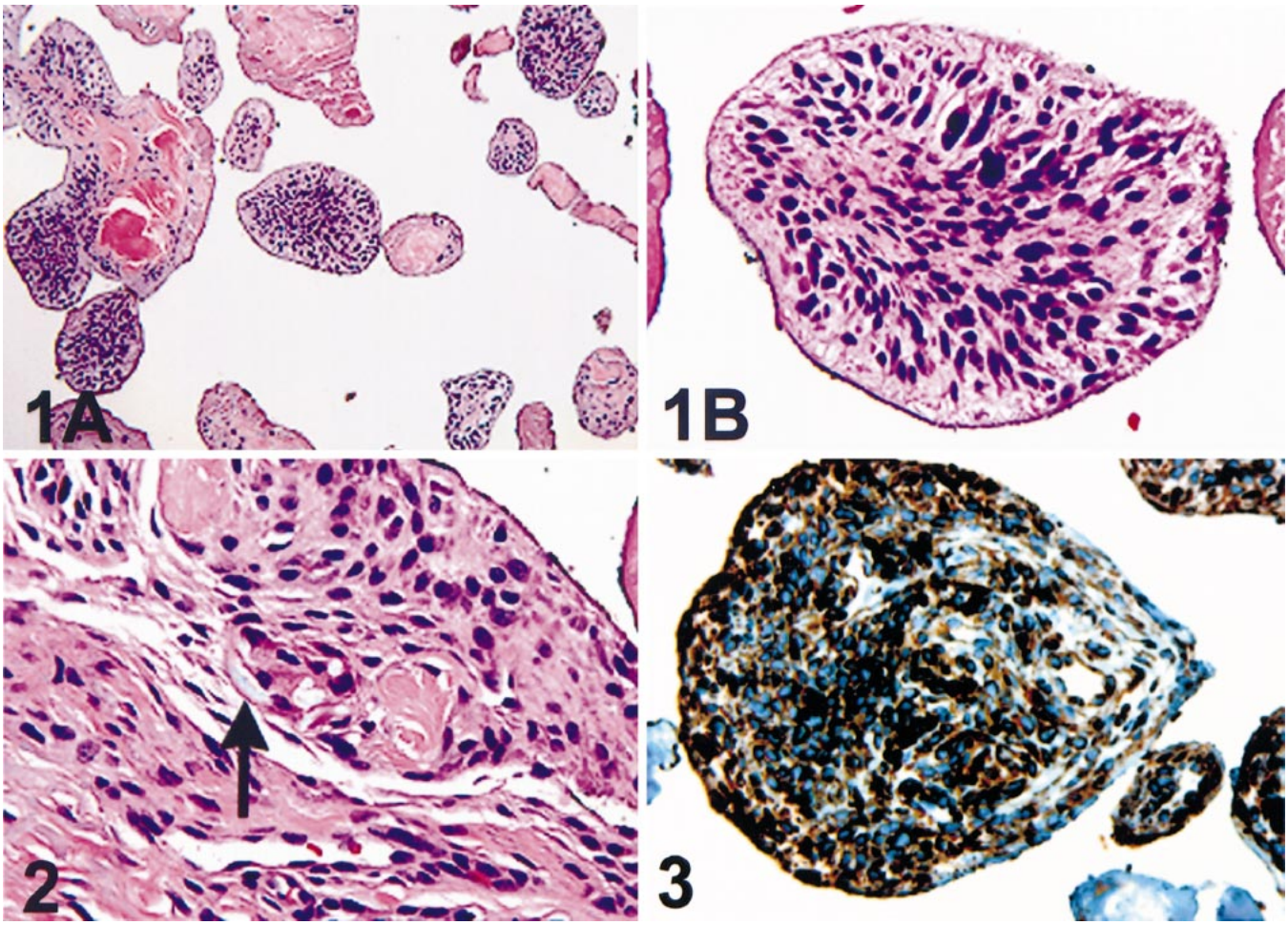


**Figure 1.** *Histologic appearance of papillary synovial metaplasia. A, Partially sclerotic papillary fronds of metaplastic tissue (hematoxylin-eosin, original magnification ×10). B, Papillae with characteristic perpendicularly oriented fibroblast-like type B synoviocytes (hematoxylin-eosin, original magnification ×40).*

**Figure 2.** *Giant cell containing polarizable material (arrow) in metaplastic tissue (partially polarized) (hematoxylin-eosin, original magnification ×40).*

**Figure 3.** *Immunohistochemical stain for vimentin with strong staining of all cells within papillae (original magnification ×40).*

(Figure 1). The papillae were composed primarily of elongated cells (fibroblast-like type B synovial cells[10]). These cells had moderate amounts of cytoplasm and had a characteristic perpendicular orientation to the surface. Between the type B synoviocytes, there were scattered single or small groups of more rounded epithelioid cells (macrophage-like type A synovial cells[10]) with moderate amounts of cytoplasm and small round to oval nuclei with generally inconspicuous nucleoli. These cells were occasionally multinucleate and rarely contained foreign material (Figure 2). Small amounts of fibrin were focally present on the surface. Some of the papillae were sclerotic. Both the epithelioid and the more elongate cells were strongly positive for vimentin (Figure 3), and rare epithelioid cells were positive for CD68 and S100. All cells were negative for pan-keratin.

## COMMENT

Normal synovial spaces form in the fetus in loose areolar tissue located between the ends of developing bones.[11] These spaces subsequently become lined by a synovial membrane. In the adult, normal synovium is composed of at least 2 types of cells. The type A synoviocytes appear to be macrophages derived from bloodborne mononuclear cells. They stain with immunostains directed against macrophages and macrophage-derived substances. The ultrastructure is similar to that of other macrophages (numerous large vacuoles, lysosomes, micropinocytotic vesicles, surface microvilli and microplicae, prominent Golgi, and small amounts of rough endoplasmic reticulum), and they have been shown to ingest foreign particles placed in joint spaces. The type A cell favors superficial locations on or near the synovial lumen. The origin of the type B synoviocytes is unknown, but they appear to be a specialized form of fibroblast. The ultrastructure of the type B synoviocyte is similar to that of fibroblasts/myofibroblasts (abundant rough endoplasmic reticulum; bundles of microfilaments and intermediate filaments, especially close to the cytoplasmic membrane; a less prominent Golgi; and fewer vacuoles and vesicles than the type A synoviocytes). A specific marker for type B synoviocytes has not been identified, although it does stain with antibodies directed against Mab 67, prolyl hydroxylase, vascular adhesion molecule 1 (VCAM-1), uridine diphosphoglucose dehy-

| Human Conditions Associated With Synovial Metaplasia | |
|---|---|
| **Condition** | **Source** |
| Next to joint prostheses | Kaufman et al,[1] Goldring et al[2] |
| Next to tendon prostheses | Hunter et al[3] |
| Next to breast prostheses | Abbondanzo et al,[4] Copeland et al,[5] Hameed et al,[6] Luke et al,[7] Raso et al,[8] Wagner et al,[9] and others |
| Next to a testicular prostheses | Abbondanzo et al[4] |
| Next to subcutaneous expander, excision of giant hairy nevus | Raso et al[8] |
| Case 1, nodule in scar of pacemaker implantation | Gonzales et al[15] |
| Case 2, appendectomy scar | |
| Case 3, laparotomy scar (for adhesion lysis) | |
| Case 1, burn scar | Beham et al[16] |
| Case 2, next to a soft tissue stone that formed after knee trauma | |
| Case 1, finger in a fisherman, no known injury | Bhawan et al[17] |
| Case 2, next to a splinter | |
| Case 3, laparotomy scar | |
| Case 4, next to a basal cell carcinoma, site not stated | |
| Scar of upper arm after removal of rheumatoid nodule | Gomez Dorronsoro et al[18] |
| Within a recurrent lipoma | Michal and Zámecník[19] |
| Next to silastic expander used in staged excision of nevus sebaceus | Stern and Sexton[20] |
| Silicone low-pressure voice prosthesis | Current case |

drogenase (an enzyme in hyaluronin synthesis), and protein gene product 9.5 (a neuron-specific ubiquitin C-terminal hydrolase). The type B synoviocyte may be distinguished histologically from fibroblasts in the surrounding tissue by the unique perpendicular orientation of the cells and their processes to the synovial lumen. Ultrastructurally, the cells have long processes that extend to the surface, ramifying into dendritic processes forming a loosely arranged plexus of interdigitating processes that, with extracellular matrix, form the surface ''membrane.'' In contrast to epithelial surfaces that line other body spaces, the synovial membrane lacks intercellular junctions between its constituent cells and lacks a well-defined basement membrane.[12] These type B synoviocytes also are known to secrete proteoglycans into the joint spaces, which are thought to serve a lubricating function for the joint.[3]

The formation of tissue having the morphologic appearance of synovium away from joint spaces was first described in the subcutaneous tissues by investigators working on inflammatory reactions to injected foreign substances[13] and later as a reaction to a subcutaneous injection of air alone.[14] In both cases, air was injected into subcutaneous tissues, where it formed a symmetrical ellipsoidal air space. In the former case this procedure was followed by injections of croton oil and/or hydrocortisone, and in the latter case only by enough air to maintain the size of the original ellipsoid. Since these original studies in experimental animals, human cases of synovial metaplasia have been described in many areas (Table). Not surprisingly, the first human cases were descriptions of the formation of synovial-like membranes reported by investigators studying the reaction of the periarticular tissues to joint and tendon prostheses.[2,3] In both cases, the synovial-like membrane formed away from the joint cavity. Rather than forming against a bubble of air, these synovial linings formed against the foreign prostheses or the substances used to cement the prostheses to the bone. In humans, the recognition that this process could occur away from joints was first made by Gonzales et al,[15] who reported the occurrence of synovial metaplasia occurring in the skin in healed surgical scars. Since then, additional cases have been reported in the skin and subcutis.[8,16–20] Most of these cases involved patients with histories of previous surgery or traumatic injuries. Although not mentioned in the reports, it is likely, at least in the surgical cases, that suture material provided a surface against which the synovial-like membranes formed. In 2 cases, tissue expanders had been placed as part of staged resections of skin lesions, providing good surfaces against which the membranes could form.[8,20]

Many of the earlier reports of silicone breast implants focused on the density of the fibrous capsule and gave only brief descriptions of the surface facing the implant.[9] In 1994, Copeland et al[5] recognized the similarity of synovial membranes to the membranes abutting silicone breast prostheses. Since then, there have been numerous reports of synovial metaplasia occurring adjacent to silicone breast implants and expanders. The metaplasia occurs both in implants filled with silicone gel and those filled with saline. Although apparently more common in patients with textured implants, synovial metaplasia also occurs with the smooth implants. We report yet another surface against which synovial metaplasia may occur, namely, silicone voice prostheses.

The literature contains much discussion concerning whether the membrane that forms in these circumstances is a ''true synovial membrane.'' Studies comparing the breast capsular membranes to synovial membranes found in villonodular synovitis have shown similar histologic, histochemical, immunohistochemical, and both transmission and scanning electron microscopic appearances.[6] Unfortunately, there are no unique and specific markers for synovial cells. Until a specific marker becomes available, it is reasonable to assume that this membrane is synovial metaplasia.

The other major discussion has centered on the cause or causes of synovial metaplasia. There is a consensus that movement is important. Drachman et al[11] demonstrated that movement of a limb is necessary for the formation of normal joint spaces that are lined by synovium. The authors also named 2 other rarely cited factors necessary for the formation of normal joint spaces: loose areolar tissue that would develop spaces secondary to the movement and relatively smooth gliding surfaces (cartilaginous caps

of bone) that would resist penetration by growing fibroblast processes. It is likely that these smooth gliding surfaces that resist penetration by fibroblast processes play a part in many of the reported cases of metaplasia, including our case.

Most of the reported cases would contain a gliding surface that would resist penetration by fibroblasts and that would be generated during a repair process. In some cases, it would be silicone prostheses (breast and soft tissue implants and expanders, artificial tendons, voice prostheses, etc). In other cases, it might be elongate-impervious sutures or the smooth surface of a splinter. In experimental cases, it might be the smooth gliding surface of an air bubble in the subcutaneous tissue that glides over the surface as the animal moves. As the fibroblast extends its process to bridge the gap formed by the original insult, it meets the impenetrable surface and turns along the surface in an attempt to find another area to bridge the gap. Being unsuccessful, it might send yet another process out, which would meet the same fate. This would result in the intertwining surface processes so characteristic of the synovial membrane. Whether the surface is smooth or papillary might depend on the surface against which the metaplasia forms or might be in response to other factors involved in the repair process. The number and location of the type A synoviocytes would be a function of that same repair response. The macrophage-like synoviocytes would be expected to be more numerous early in the repair process and to become fewer with time unless presented with additional foreign material, as in the case of leaking or weeping silicone gel–filled implants. The synovial-like orientation of the fibroblast-like synoviocytes may remain as long as the gliding movement of the foreign material keeps the potential space open. Once contraction of other elements of the joint capsule restricts the movement of the foreign material, the fibroblast may not be able to detect a space that would need closing and would then remodel the tissue so that the synoviocytes are oriented parallel or randomly to the surface and would lose the unique features that would identify this membrane as a synovial-like membrane. Thus, it might be that synovial metaplasia is a unique morphologic variant of the repair process that occurs under specific physical circumstances. Even though this theory would explain many of the cases described in the literature, there are rare cases that do not fit the pattern (case 1 cited by Beham et al[16] and cases 1 and 4 cited by Bhawan et al[17]). Thus, additional unknown factors might play a role in some cases.

**References**


1. Kaufman RL, Tong I, Beardmore TD. Prosthetic synovitis: clinical and histologic characteristics. *J Rheumatol.* 1985;12:1066–1074.
2. Goldring SR, Schiller AL, Roelke M, Rourke CM, O'Neill DA, Harris WH. The synovial-like membrane at the bone-cement interface in loose total hip replacements and its proposed role in bone lysis. *J Bone Joint Surg Am.* 1983;65:575–584.
3. Hunter JM, Jaeger SH, Matsui T, Miyaji N. The pseudosynovial sheath: its characteristics in a primate model. *J Hand Surg.* 1983;8:461–470.
4. Abbondanzo SL, Young VL, Wei MQ, Miller FW. Silicone gel-filled breast and testicular implant capsules: a histologic and immunophenotypic study. *Mod Pathol.* 1999;12:706–713.
5. Copeland M, Choi M, Bleiweiss IJ. Silicone breakdown and capsular synovial metaplasia in textured-wall saline breast prostheses. *Plast Reconstr Surg.* 1994;94:628–636.
6. Hameed MR, Erlandson R, Rosen PP. Capsular synovial-like hyperplasia around mammary implants similar to detritic synovitis: a morphologic and immunohistochemical study of 15 cases. *Am J Surg Pathol.* 1995;19:433–438.
7. Luke JL, Kalasinsky VF, Turnicky RP, Centeno JA, Johnson FB, Mullick FG. Pathological and biophysical findings associated with silicone breast implants: a study of capsular tissues from 86 cases. *Plast Reconstr Surg.* 1997;100:1558–1565.
8. Raso DS, Greene WB, Metcalf JS. Silicone breakdown and clinical implications of mammary and extramammary synovial metaplasia in periprosthetic capsules. *Plast Reconstr Surg.* 1995;96:1747.
9. Wagner H, Beller FK, Pfautsch M. Electron and light microscopy examination of capsules around breast implants. *Plast Reconstr Surg.* 1977;60:49–55.
10. Barland P, Novikoff AB, Hamerman D. Electron microscopy of the human synovial membrane. *J Cell Biol.* 1962;14:207–220.
11. Drachman DB, Sokoloff L. The role of movement in embryonic joint development. *Dev Biol.* 1966;14:401–420.
12. Iwanaga T, Shikichi M, Kitamura H, Yanase H, Nozawa-Inour K. Morphology and functional roles of synoviocytes in the joint. *Arch Histol Cytol.* 2000;63:17–31.
13. Selye H. On the mechanism through which hydrocortisone affects the resistance of tissues to injury: an experimental study with the granuloma pouch technique. *JAMA.* 1953;152:1207–1213.
14. Edwards JCW, Sedgwick AD, Willoughby DA. The formation of a structure with the features of synovial lining by subcutaneous injection of air: an *in vivo* tissue culture system. *J Pathol.* 1981;134:147–156.
15. Gonzales JG, Ghiselli RW, Santa Cruz DJ. Synovial metaplasia of the skin. *Am J Surg Pathol.* 1987;11:343–350.
16. Beham A, Fletcher CDM, Feichtinger J, Zelgar B, Schmid C, Humer U. Synovial metaplasia of the skin. *Virchows Archiv A Pathol Anat Histopathol.* 1993;423:315–318.
17. Bhawan J, Dayal Y, Gonzales-Serva A, Eisen R. Cutaneous metaplastic synovial cyst. *J Cutan Pathol.* 1990;17:22–26.
18. Gomez Dorronsoro ML, Martinez-Peñnuela JM, de la Hermosa JR. Metaplastic synovial cyst. *Am J Surg Pathol.* 1988;12:649–650.
19. Michal M, Zámecník M. Synovial metaplasia in lipoma. *Am J Dermatopathol.* 1998;20:285–289.
20. Stern DR, Sexton FM. Metaplastic synovial cyst after partial excision of nevus sebaceous. *Am J Dermatopathol.* 1988;10:531–535.