Original Article

Infection associated with hydroxyapatite prosthesis and related factors

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Background The purpose of otomicrosurgery in modern times is to achieve complete removal of disease, which is the basis for hearing rehabilitation. Artificial ossicles are important for hearing rehabilitation. One of the materials is hydroxyapatite that acts as ossicular replacement prosthesis (HA prosthesis, PORP & TORP) and is commonly used as substitute bone in clinics. Although HA prostheses feature good biocompatibility, stability and certain resistance to infection, the structure of the material can be decomposed and absorbed. Based upon animal experiments and clinical application, this article explores the infectivity of HA prostheses and influencing factors.

Materials and Methods HA prostheses were implanted in the bulla in guinea pigs. Infected HA prostheses were examined under a scanning electron microscope. Ninety patients implanted with HA prostheses were followed for more than 3 months. Five cases that had undergone revision operations were reported. Results Scanning electronic microscopy showed that the normal compact structures had disappeared and become loose in infected HA prostheses, with their micropores infiltrated with effusion, fibrous tissue and inflammatory cells. As a result, the normal ceramic structure was decomposed and the micropores structure disappeared. The infected mesotympanum in the reported cases also led to HA infection. The shape and structure of bone were destroyed, which was visible by visual examination and light microscopy. The process of cholesteatoma recurrence was always associated with infection, although the HA prosthesis was sometimes spared. Conclusion While HA prosthesis is anti-infective to some extent, long-term infection and cholesteatoma recurrence can lead to destruction and decomposition of HA prostheses. Long-term infected middle ear cavity, dysfunctional Eustachian tube, residual and recurrent cholesteatoma and other factors can cause decomposition of HA prosthesis and result in hearing loss.

Key words Hydroxyapatite prosthesis, Infection, Cholesteatoma.

Introduction The purpose of otomicrosurgery in modern times is to achieve complete removal of disease, which is the basis for hearing rehabilitation. Ninety HA prostheses (PORP & TORP) have been implanted by the authors in cases of chronic otitis media and cholesteatoma otitis media to rebuild the ossicular chain since 2005. This paper intends to review animal experiment data and 5 cases of HA infection for the purpose of extending understanding of the prosthesis material itself and factors related to its infection.

Materials and methods

Animal experiments

Twelve healthy white guinea pigs (200–250 g) (24 ears) were used. Normal prayer’s reflex was confirmed. Under general anaesthesia with peritoneal administration of 2% sodium pentobarbital (4 mg / 100 g), an incision was made over the bulla bilaterally under aseptic conditions, and the HA prosthesis was implanted. After 3–4 months, three guinea pigs were decapitated and the bulla removed. The surface of the implant and surrounding tissues were examined under an electron microscope. The HA material is US Food and Drug Adminis-
Clinical data

A total of 90 HA prostheses had been implanted during middle ear surgeries since 2005 in patients aging from 11 to 65 years (41 males and 49 females). The course of the diseases was from 3 months to 40 years. Simple tympanoplasty was conducted in 12 cases of chronic suppurative otitis media. Mastoidectomy and tympanoplasty were performed in 78 cases of cholesteatoma otitis media: intact–bridge mastoidectomy with tympanoplasty (IBM) in 45 cases, canal wall down procedures in 8 cases and canal wall up with epitympanoplasty in 25 cases. The mastoid cavity in all 78 cases was obliterated with bone meal. All cases were followed up for more than 3 months. Eight of these cases had revision operations, of which 5 were described in this paper.

Results

Animal experiment results

All 12 guinea pigs recovered well from surgeries. Six ears in three guinea pigs were inspected at one to four months post–surgery. One implanted cavity in Guinea Pig No 3 was infected during the first month after surgery and the infected bulla was filled with fibrous adhesion tissue and crisp bones, consistent with chronic bone inflammation. The implanted HA prosthesis appeared dark, contaminated and fragile, with indistinguishable boundary from surrounding tissues. Under the electronic microscope (Figure 1), the organizational structure of normal dense granules had disappeared, replaced by a loose structure with infection cavities. Micropores of the HA was infiltrated by effusion, fibrous tissue and inflammatory cells. As a result, the normal ceramic structure was decomposed and the porous structure disappeared. In the rest 23 ears with no signs of infection, good bone structure was observed on electronic microscopy (Figure 2).

Clinical data

HP prosthesis infection

Case 1: A 46 years old male received mastoidectomy with tympanoplasty in 2006 for chronic suppurative otitis media. An HA–Plastipore (PORP) was used to reconstruct the ossicular chain during the procedure. The ear continued to drain with no hearing recovery following the surgery. In February 2009, a revision operation was performed with the following findings: the pars flacida was retracted and draped around the PORP which was surrounded by granulation, fibrous hyperplasia tissues and thick purulent fluid; the horizontal and the second section of the facial nerve were exposed, although with no facial paralysis; the attic lateral wall had collapsed with no cholesteatoma; the implanted HA prosthesis appeared yellow and surrounded by inflammation tissues. During the revision operation, the HA–PORP was replaced. At one year followed up, there was no sign of recurrence and hearing remained unchanged from that of

![Figure 1](image1.png)

**Figure 1** Scanning electronic microscopy showing loss of normal organizational structure of dense granules in an HA prosthesis which has become loose. Transuding contexture, fibrous tissue and inflammatory cells infiltrated in the HA pores (white arrow). Normal ceramic structure decomposition (red arrow).

![Figure 2](image2.png)

**Figure 2** The inner organization of an implanted part that remains intact and shows clear boundaries (white arrows) on scanning electronic microscopy. HA particles and pores of surface structures are in good condition (red arrow). It possesses no leaking organizations, fibrous tissue or inflammatory cell infiltration.
pre-operative level. Figure 3 shows the removed HA–PORP.

Case 2: A 60 male received a tympanoplasty and HA prosthesis implantation in his left ear for chronic suppurative otitis media in 1992. Dry ear and hearing improvement were obtained after surgery. Otorrhea recurred in 2008. Examination revealed a red rice-size granulation tissue on the surface of the eardrum, small amount of bloody otorrhea in the ear canal, dark red tympanic membrane and dysfunctional Eustachian tube. A revision procedure was performed in February 2010, which showed cholesterol granuloma in the mastoid cavity, antrum and epitympanum. The previously implanted HA prosthesis was dark brown in color, crisp and deformed. Its remnant was indistinguishable from the surrounding cholesterol granulation tissue. Histological examination indicated inflammatory changes in the HA bone. A titanium prosthesis was implanted, but hearing was unchanged postoperatively.

Recurrence of cholesteatoma

Case 3: A 29 years old man, received an IBM operation on December 11, 2007, for cholesteatoma otitis media. Intact bridge mastoidectomy was performed to remove disease. The mastoid cavity and attic was closed with bone meal and the ossicular chain was reconstructed with HA–PORP. The operative cavity healed one month later. In Dec 2008, due to persisting otorrhea, he was hospitalized and found to have large amount of debris and inflammatory exudates in the operative cavity. A thorough debridement revealed intact tympanic membrane and collapsed attic, but no cholesteatoma. In Sep 2009, he was examined again for bloody otorrhea. At this time, the attic, which was separated from the antrum and middle ear cavity, remained open to the ear canal. Another round of debridement was performed. One year later, the ear was reexamined and otoendoscopic findings are shown in Figure 4. The air–bone gap over speech frequencies (0.5, 1 and 2 kHz) was 12 dB HL pre-operatively. Three months and two years later, the hearing level remained at the same level.

Case 4: A 21 years old female received the same operation for the same disease as in Case 3 on July 21, 2006. After an intact bridge mastoidectomy, a HA–PORP was used to reconstruct the ossicular chain. The operative cavity healed one month later with hearing improvement. In June 2009, the ear started to drain again with no hearing change. Examination showed a retraction pocket in the attic area with formation of cholesteatoma. The pars tensa remained intact, and the HA–PORP (Figure 5) was visible under the tympanic membrane. CT examination confirmed the presence of the PORP (Figure 6). On September 10, 2009, a revi-

![Figure 3](image1.png) **Figure 3** HA–plastipore prosthesis photographed during the operation in Case 1. The black arrow indicates HA top plate infection, characterized by pale brown color and losing boundaries with the surrounding tissue. The shape of HA bone is unrecognizable. The inset shows the enlarged HA prosthesis, with the white arrow pointing to the HA part of prosthesis with dark brown and surrounding granulation tissue. **Figure 4** Well healed tympanic membrane (white arrow) one year after operation in Case 3. Some secretions and cholesteatoma crusts are visible in the attic (dark arrow).
sion operation showed that the cholesteatoma and granulation tissue in the attic had partly eroded the graft material in the epitympanum from the previous operation. Histological report indicated bone tissue with inflammatory changes. The mastoid cavity remained clear and the fibrous tissue near the HA–PORP contained no cholesteatoma, the joint between PORP and the head of stapes connected well, but the HA prosthesis had slipped. The mucosa in the middle ear cavity was normal. After disease removal, the position of HA bone was adjusted and temporal fascia was used to cover the attic. The ear dried up in one month. The air–bone gap over speech frequencies improved from 40 dB pre-operatively to 20 dB at one year postoperatively and 15 dB three years later.

Case 5: A 29 years old female received the same operation in September 2007 for the same diagnosis as in Case 3. In July 2009, a pocket retraction, crust of cholesteatoma and purulent secretion was found in the attic upon otoendoscopic examination. In August 2009, large amount of pus was drained from under the skin of posterior canal wall while the pars tensa remained intact. CT examination revealed HA prosthesis displacement (Figure 7). A revision procedure showed that the HA–PORP had been pushed backwards by the cholesteatoma lump and dislocated from the head of stapes, but with no infection (Figure 8). Histological examination showed signs of inflammatory bone ossification in the mastoid cavity (Figure 9). Following debridement, the position of the HA prosthesis was adjusted and the epitympanum was obliterated with bone meal. One month later, the attic, separated from the antrum and mesotym-
panum, was sunken again but open to the external ear canal. Speech frequency AB gap was 20 dB before the first surgery and 30 dB two years later (before the revision operation).

**Discussion**

**Anti-infectiveness of HA materials**

From the seventies of last century, HA prostheses have been used and become the most widely used bone material. Goldenberg (2001) reported that, based upon the results from the Association of Otology and Association of the Neural Science of the United States, hydroxyapatite materials ranked at the top on the usage list [1]. HA prostheses feature good biocompatibility and stability with some resistance to infection. But compared with the titanium prosthesis, the structure of HA prostheses can be decomposed and absorbed when the middle ear contains high level of persisting infection.

In our animal study, the bulla cavity was found to be filled with fibrous tissue with bone degradation consistent with chronic inflammation on scanning electron microscopy in one animal with post-operative infection (Guinea Pig No.3) (Figure 1). The boundary between the implant and the surrounding tissue was unclear and the surface of hydroxyapatite organizations appeared rough under the electron microscope, with inflammatory tissue infiltrated into the hydroxyapatite pores. All these findings suggest degradation of the implanted material [2]. Blitterswijk (1990) reported that the micropores of HA prosthesis, when infected, were filled with bone-like and fibrous tissue under light and electron microscopes. Infection accelerates HA degradation significantly [3]. For this reason, most of prosthesis materials used in Europe are titanium, (such as Germany KURZ titanium prostheses). In the United States, there is also a trend toward using titanium. Fig. 2 shows the normal structure organization of HA prostheses.

**Factors leading to middle ear infection**

In our cases, the HA prosthesis in Case 1 was in the state of decomposition after being infected due to incomplete clearance of middle ear disease in the operation. Gross visual examination of the HA showed obvious signs of infection (Figure 3). In Case 2, dysfunction of the Eustachian tube and long-term negative pressure in the middle ear cavity led to cholesterol granuloma formation, resulting in infection of the HA prosthesis.

Histology report on the HA prosthesis in Case 2 showed inflammatory cells infiltrating HA micropores, which explains HA degradation and the resultant hearing loss. Vrabec (2002) reported that extrusion of HA prosthesis was closely related to recurrence of middle ear disease, tympanic membrane inflammation and tympanic membrane retraction [4]. One possible solution to this problem is placing a piece of sliced cartilage graft between the top plate and the tympanic membrane [5]. Rondini–Gilli (2003) reported that extrusion rate of HA was 2% and the displacement rate was 10% in 100 cases (65 cases with HA–PORP and 35 cases with HA–TORP) at 1 year followed up [6].

–Formation of retraction pockets in the attic as a related infective factor

Mucus secretion and fibrosis in the middle ear cavity can lead to blockage of communication to the attic which can contribute to the formation of local negative pressure. The pars flacida of tympanic membrane that lacks of fiber layer will be drawn in to form retraction pockets, leading to the formation of epithelial accumulation called cholesteatoma which have different impacts on the HA prosthesis at different stages of cholesteatoma development.

The mastoid cavity and epitympanum was filled with bone meal and covered with skin and fascia after the disease was removed in Cases 3, 4 and 5 in IBM surgeries. Because the bone meal did not undergo complete ossification or there was bone resorption after ossification (no
bone bridge in the revision surgery), retraction of fascia with the formation of hyperkeratosis epithelium accumulation on its surface followed. Another potential cause was that poor blood supply to the bone and fascia had impaired healing. Because of the infection and attic retraction, cholesteatoma formed and eventually affected the antrum and mastoid cavity.

The normal skin shedding can lead to accumulation of epithelial debris followed by formation of cholesteatoma and infection. In Case 3, because the sunken attic was isolated from the antrum and the mesotympanum and open to the external auditory canal, cleaning of cholesteatoma matrix was easy and there was no effect on HA prosthesis and hearing.

In Case 4, the attic retraction pocket extended to the antrum. Due to infection and the erosion of bone ossification, the filling materials applied during the previous surgery showed signs of bone inflammation, although there was not yet infection with the HA prosthesis. As a result, hearing was not affected.

The causes for cholesteatoma formation in Case 5 were the same as that in Case 4, except that the lesion involved the entire mastoid cavity giving rise to infection, but the HA prosthesis in this case showed resistance to infection.

The clinical and histological findings in Cases 3, 4 and 5 are consistent with the speculation on attic retraction pockets and cholesteatoma formation process reported by Sudho in 2007 based upon immunohistochemistry studies, i.e.: the retraction pockets develop first, followed by epithelial overgrowth in the pockets (including the formation and accumulation of keratosis materials) and finally attic cholesteatoma expansion and resultant bone inflammation and resorption. Therefore, when attempting cholesteatoma eradication and hearing reconstruction, the attic should be effectively dealt with to prevent recurrence of cholesteatoma that will affect the HA prosthesis.

**Conclusion**

HA bone has been one of the widely used prostheses for hearing reconstruction. With certain levels of resistance to infection, HA prostheses feature good biocompatibility and stability even in the presence of long-term infection. However, the structure of the material can be decomposed and absorbed. Long-term middle ear infection, Eustachian tube dysfunction, residual and recurrent cholesteatoma and other factors in the surgery of the middle ear can cause decomposition of HA bone, which will result in loss of hearing.

**References**