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Main Article

Differentiation between cholesteatoma and inflammatory process of the middle ear, based on contrast-enhanced computed tomography imaging

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Abstract

Objective: to assess the usefulness of delayed post-contrast computed tomography (CT) examination for the detection of residual or recurrent cholesteatoma after canal wall up tympanoplasty.

Study design and setting: This prospective, non-randomized study, set within an academic medical centre, included 17 consecutive patients who had undergone canal wall up tympanoplasty for cholesteatoma, with possible recurrence. Pre-contrast CT scans and delayed post-contrast images were compared with second look surgical findings.

Results: A residual or recurrent cholesteatoma was found in eight of the 17 patients at revision surgery and was correctly diagnosed on post-contrast CT images in six patients (75 per cent). In the two misdiagnosed cases, cholesteatoma pearls smaller than 2.5 mm were not seen on post-contrast CT. The sensitivity of the imaging test was 75 per cent, the specificity was 60.1 per cent, the positive predictive value was 88.1 per cent and the negative predictive value was 81.8 per cent.

Conclusion: Computed tomography with delayed post-contrast images is a sensitive imaging modality for the detection of residual cholesteatoma. If proven reliable, this method of non-invasive imaging could spare the patient unnecessary revision surgery.

Key words: Cholesteatoma; Tomography, Computed; Otologic Surgical Procedures; Tympanoplasty

Introduction

Canal wall up tympanoplasty has become a major surgical treatment for acquired cholesteatoma of the middle ear. Although it has many advantages, this procedure also has some disadvantages. One of these is the need for 'second look' surgery following the initial procedure, considered mandatory in modern otological practice by many authors.[1,2]

Since such second look surgery is an invasive procedure, imaging is increasingly taking its place in the follow up of such patients, in an attempt to detect residual cholesteatoma and thus avoid unnecessary surgery. In the past decades, several studies evaluated the contribution of both magnetic resonance imaging (MRI) and computed tomography (CT) imaging in detecting residual or recurrent cholesteatoma. These authors stated that neither conventional CT[3,4] nor MRI[5] was able to confidently detect the presence of cholesteatoma, especially when the post-operative cavity was almost completely opacified. Improvement in imaging techniques have generated new data on the usefulness of MRI in detecting residual cholesteatoma. It is now known that MRI examination with the use of delayed, contrast-enhanced, T1-weighted images has very good results in the detection of post-operative residual cholesteatoma.[5–11] Rapid technical progress in CT imaging has also been achieved. However, to date, no studies have addressed the usefulness of modern CT imaging methods in the investigation of recurrent or residual cholesteatoma.

The purpose of this study was to determine whether modern contrast-enhanced CT imaging could detect post-operative recurrent or residual cholesteatoma.

Patients and methods

From June 2003 to April 2005, 39 patients who had previously undergone canal wall up tympanoplasty for acquired middle-ear cholesteatoma underwent a follow-up CT examination in our radiology department. The mean time interval between the canal wall up tympanoplasty and the follow-up CT was 14 months. Seventeen patients (11 men, six women; age range 43–59 years; mean age 49 years) were found to have partial or complete opacification of

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the tympanomastoid cavities on CT and thus (prospectively) underwent specially designed, contrast-enhanced CT examination. Second look surgery was performed in all these patients within nine weeks of the contrast-enhanced CT. In the remaining 22 patients, the CT demonstrated either the absence of intratympanic opacity (19 patients) or clear evidence of cholesteatoma recurrence (two patients). These patients were excluded from further contrast-enhanced CT examination.

Imaging technique and post-processing

High resolution, multislice CT examination of the temporal bones was performed using a LightSpeed Ultra Advantage eight-row unit (GE Healthcare, Milwaukee WI, USA) with the following parameters of acquisition: slice thickness 0.6 mm, slice overlap 0.3 mm, 120 kVp and 180 mAs. A 96 mm acquisition field of view was used separately for each temporal bone, with a 512 × 512 matrix. Both soft tissue and bone reconstruction algorithms were applied. After intravenous injection of 60 ml of iodine-non-ionic contrast medium (Visipaque, GE Healthcare, Milwaukee, Visconsin, USA) in a 1.5 ml/s bolus, CT examination was performed again. Delayed contrast-enhanced CT images were finally obtained with a delay range of 300–360 seconds (5–6 minutes) after contrast administration. The source images were then transferred onto a separate workstation and processed with the standard Reformat tools and Navigator virtual endoscopic software (GE Healthcare; Advantage Workstation 4.2) in order to obtain multiplanar and curved two-dimensional reformations and also three-dimensional reconstructions with virtual endoscopic views.

Image interpretation

All images were analysed independently by two experienced head and neck radiologists who were blinded to patients' data and second look surgical findings. The initial CT and contrast-enhanced CT images were separately evaluated by the same observers. Interpretation was based on the density, expressed in Hounsfield units, of the soft tissue mass within the post-operative cavity. A comparison of the mass density before and after contrast administration was performed. In order to facilitate this comparison, different Hounsfield unit values were colour-coded and colour maps of density were created. Residual or recurrent cholesteatoma was diagnosed if a non-enhancing mass was visible in the tympanomastoid cavity. Post-operative granulation tissue was diagnosed if significant enhancement of the mass (exceeding 10 Hounsfield units) was observed.

Statistics

For each observer, sensitivity, specificity and predictive values were separately evaluated for the initial CT and the contrast-enhanced CT images, compared with the results of second look surgery. Mean values for the two observers were calculated for each parameter. Inter-observer agreement between imaging findings and the results of surgery were evaluated using Cohen kappa statistics.

Results

A residual or recurrent cholesteatoma was diagnosed in eight of the 17 patients at revision surgery. Cholesteatoma was correctly detected in six cases (75 per cent) on delayed post-contrast CT images. Residual or recurrent cholesteatomas presented typically as lobulated or nodular masses of a soft tissue density, and they were found in the cavum tympani (50 per cent), the mastoid cavity (37.5 per cent) or both (12.5 per cent). On pre-contrast CT scans, both cholesteatoma and granulation tissue appeared slightly hypodense. On delayed post-contrast images, cholesteatomas showed no significant change in density (Figure 1), whereas granulation tissue revealed significant contrast enhancement (Figure 2).

In the six correctly diagnosed cases of recurrent cholesteatoma, the mean enhancement value was 0.5 Hounsfield units (range, 0–3 Hounsfield units). In the remaining cases, diagnosed as granulation tissue, the enhancement ranged from 18 to 26 Hounsfield units (mean, 21 Hounsfield units). In two patients, cholesteatoma pearls identified during surgery were not diagnosed on contrast-enhanced

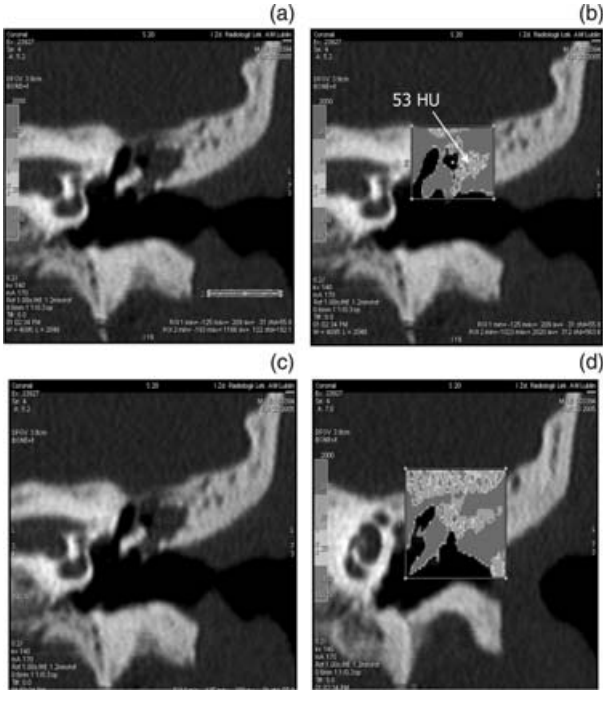

FIG. 1

Residual cholesteatoma 11 months after canal wall up tympanoplasty. (a) Pre-contrast coronal computed tomography (CT) scan demonstrates opacity of the tympanomastoid cavity. (b) Colour-coded density map demonstrates the mean density of the mass (53 Hounsfield units). (c) Delayed post-contrast coronal CT scan shows no visible central enhancement of the soft tissue mass. (d) No enhancement is visible on the colour-coded density map.

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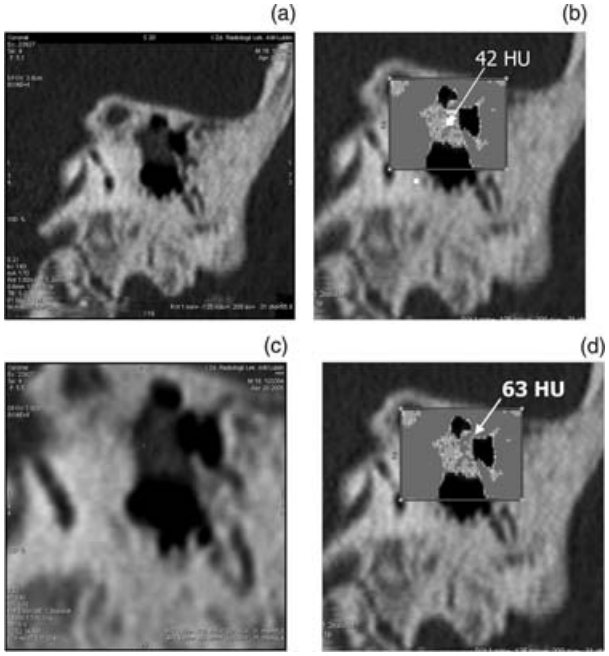

FIG. 2

Post-operative granulation tissue 14 months after canal wall up tympanoplasty. (a) Pre-contrast sagittal computed tomography (CT) scan demonstrates partial opacity of the tympanomastoid cavity. (b) Colour-coded density map demonstrates the mean density of the mass (42 Hounsfield units). (c) Delayed post-contrast axial CT scan shows significant enhancement of the soft tissue mass. (d) Enhancement is clearly visible on a colour-coded density map, especially in its central portion.

CT examination. This might have been due to their small size (not exceeding 2.5 mm). There was one false positive case in which granulation tissue revealed no significant contrast enhancement (7 Hounsfield units) and was misdiagnosed as a cholesteatoma. This could possibly be explained by the much greater time required in this case to observe strong, homogenous enhancement, typical for granulation tissue.

The smallest residual cholesteatoma detected at CT examination measured 4 mm. The diameter of other lesions ranged from 5 to 23 mm. Agreement between observers was very good for the comparison of pre-contrast with contrast-enhanced images (kappa 0.73–1, mean 0.85). Sensitivity, specificity, and positive and negative predictive values are presented in Table I.

TABLE I

USEFULNESS OF CONVENTIONAL PLUS CONTRAST-ENHANCED CT IMAGES IN DETECTING RESIDUAL/RECURRENT CHOLESTEATOMA, COMPARED WITH SECOND LOOK SURGERY

	Observer 1	Observer 2	Mean
Sensitivity (%)	75.0	75.0	75.0
Specificity (%)	59.7	61.5	60.1
Positive predictive value (%)	88.1	89.5	88.8
Negative predictive value (%)	81.8	81.8	81.8

Discussion

Canal wall up tympanoplasty is nowadays one of the major surgical techniques used to treat acquired cholesteatomas of the middle ear.[1] In this procedure, the surgeon reconstructs or preserves the posterior wall of the external auditory canal. This procedure has major advantages, such as rapid healing time, easier long term care and no need for water precautions for the patient. Also, hearing aids are easier to fit in such ears. Among the disadvantages of this method, the most important are frequently recurrent disease (compared with canal wall down tympanoplasty) and difficulties with recurrence detection.[1,5] A surgical second look operation is often necessary 12–18 months after the initial surgery in order to rule out residual or recurent cholesteatoma. A second look operation may be planned when technical conditions during the initial surgery suggest that the excision of the lesion may be incomplete; in other cases, the indication for surgical revision is based upon patient's symptoms, clinical follow up and the results of imaging studies.

A simple, non-contrast-enhanced CT examination is able to reveal either the complete absence of a soft tissue mass in the post-operative cavity or clear evidence of a cholesteatoma in the cavity, with its typical imaging features (such as nodular or lobulated shape, associated with osteolytic foci in the bony walls of the tympanomastoid cavity).[3,4] In these cases, no further imaging is required.

However, in many cases, the post-operative cavity is partially or completely filled with a soft tissue mass, and a standard CT examination cannot reliably characterize this mass.[6] Since 2003, several studies have proven that, in such cases, MRI examination allows a differentiation between granulation tissue and cholesteatoma.[6–8,10] Granulation tissue is poorly vascularized (possibly due to microvascular thrombosis); therefore, after contrast administration, the enhancement pattern will be delayed but constant and significant.[12] Conversely, the major part of a cholesteatoma is made of retained keratin, so it is strictly avascular and will show a constant lack of enhancement.[12,13] A retrospective analysis of post-contrast MRI images showed that 89 per cent of recurrent cholesteatomas identified during surgery showed no enhancement and that granulation tissue revealed in all cases a slow but constant enhancement which reached the centre of the tissue after 30–45 minutes.[6,10]

Based on the morphological features of both cholesteatomas and granulation tissue, we became interested in whether the same pattern of post-contrast enhancement would be visible on CT examination. Having had experience with the post-contrast enhancement of scar tissue on CT examination (in the case of scar developing after intervertebral disc removal and mimicking a prolapsed disc), we decided to perform post-contrast delayed images after 5–6 minutes, instead of 30–45 minutes, as described in MRI examination protocols.

All our patients underwent both pre-contrast and delayed post-contrast CT examination. Compared

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with pre-contrast CT images, post-contrast images allowed confident differentiation between cholesteatoma and granulation tissue in most cases (75 per cent). This was due to the significant contrast between homogenously enhancing granulation tissue and non-enhancing cholesteatomas on delayed post-contrast images.

Of the eight recurrent cholesteatomas revealed during second look surgery, two were false negatives based on delayed post-contrast CT examination. From our CT examinations, there was also one false positive case. The false negative cases were not noticed due to the minute size of the cholesteatoma pearls involved (2.5 mm). Such small lesions might be missed, probably due to a partial volume effect between the cholesteatoma pearls and the granulomatous tissue the pearls were embedded in. However, in our opinion, there is probably very little risk in leaving a residual cholesteatoma less than 3 mm in size within the post-operative cavity, if close clinical and imaging follow up of the patient occur. This implies that, in cases of tympanomastoid cavity opacification with no signs of cholesteatoma, several follow-up CT examinations (e.g. every four to six months) should be mandatory. The false positive case revealed no significant contrast enhancement after 6 minutes and so was diagnosed as cholesteatoma. During surgery, however, the lesion proved to be granulation tissue. The lack of enhancement could have been caused by the specific microstructure of this tissue (possibly numerous microvascular thrombosis phenomena),[12] which might have been responsible for a very slow contrast enhancement pattern. The lesion would probably have been well visualized if we had performed an additional examination after a further 25–30 minute delay. This raises the question of whether our post-contrast delay time (5–6 minutes) was sufficient to detect all cases of granulation tissue. In our opinion, this question requires further study on a larger number of patients, examining different delay times.

In conclusion, both post-contrast MRI and contrast-enhanced CT examinations may currently be considered as alternatives to a surgical second look procedure, allowing a significant reduction in cost and morbidity. However, further studies on larger series are necessary in order to confirm the reliability of these imaging techniques, before their routine implementation.

This preliminary study shows that CT examination, using delayed post-contrast images, is a reliable tool in detecting residual or recurrent cholesteatomas of the middle ear in patients who have undergone canal wall up tympanoplasty. Compared with post-contrast T1-weighted MRI, CT examination has a lower sensitivity and specificity (75 per cent compared with 85.2 per cent and 60.1 per cent compared to 92.6 per cent, respectively). However, it is important to perform a CT examination, as calcified scar nodules and ossicular elements frequently present in the post-operative cavity. The presence of diffuse calcifications may affect precise evaluation of the granulation tissue enhancement pattern on MRI; therefore, CT scans should accompany MRI scans, in order to properly assess the pathology.

When the results of this study are confirmed in a larger series, and the delayed post-contrast protocol modified accordingly, reliable post-operative follow-up of canal wall up tympanoplasty might be possible based on CT examination alone.

Summary

Imaging has an increasing role in the follow up of patients who have undergone surgery for cholesteatoma, with CT as the first line imaging technique. However, in most cases, conventional CT examination is not able to differentiate residual cholesteatoma from post-operative granulation tissue. The objective of this study was to assess the usefulness of CT examination using delayed post-contrast images for the detection of residual or recurrent cholesteatoma after canal wall up tympanoplasty, in cases in which conventional CT was not conclusive.

The study included 17 consecutive patients who had undergone canal wall up tympanoplasty for cholesteatoma and whose initial CT had shown an opacity in the tympanomastoid cavity. In all patients, delayed post-contrast CT images (5–6 minutes after contrast injection) were performed. Results were compared with surgical findings in all cases.

A residual or recurrent cholesteatoma was found in eight of the 17 patients at revision surgery and was correctly diagnosed on post-contrast CT images in six patients. In the two misdiagnosed cases, cholesteatoma pearls smaller than 2.5 mm were found. There was one false positive case. This was probably due to atypical enhancement of granulation tissue. The sensitivity of delayed post-contrast CT was 75 per cent, specificity was 60.1 per cent, the positive predictive value was 88.8 per cent and the negative predictive value was 81.8 per cent.

Based on our research, it may be concluded that CT with delayed post-contrast images is a reliable and sensitive imaging modality for the detection of residual cholesteatoma of diameter $\geq$3 mm. This non-invasive imaging method could spare patients suspected of recurrence the inconvenience of revision surgery.

- **This study aimed to assess the usefulness of delayed post-contrast computed tomography examination for the detection of residual or recurrent cholesteatoma after canal wall up tympanoplasty**
- **This prospective, non-randomized study included 17 consecutive patients after canal wall up tympanoplasty for cholesteatoma, with possible recurrence**
- **Computed tomography with delayed post-contrast images was a reliable and sensitive imaging modality for the detection of residual cholesteatoma of diameter $\geq$3 mm**
- **This non-invasive imaging method could spare patients suspected of recurrence the inconvenience of revision surgery**

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