SQUAMOUS CELL CARCINOMA ANTIGEN AS A DIAGNOSTIC MARKER OF NASAL INVERTED PAPILLOMA

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INVERTED PAPILLOMA

- INVERTED PAPILLOMA (IP) IN THE PARANASAL SINUS IS A BENIGN NEOPLASM WITH UNIQUE CLINICAL CHARACTERISTICS; IN PARTICULAR, IT HAS A HIGH RECURRENT RATE AND A MALIGNANT LESION MIGHT DEVELOP.

- 2ND MC BENIGN SINONASAL NEOPLASM, AND MC INDICATION FOR SURGERY IN BENIGN SNT

- BASED ON SEVERAL META ANALYSES,

- LOCAL RECURRENT RATE, AROUND 12%

- MALIGNANT TRANSFORMATION, AROUND 10%
WHY IT'S CALLED INVERTED?

- Arises from proliferation of squamous epithelium through finger-like projections into the underlying stroma "rather than the surface".

- One type of Schneiderian papillomas:
  - Inverted papilloma
  - Fungiform papilloma
  - Cylindrical papilloma

- Benign with locally aggressive behavior!!
IMAGING AND STAGING SYSTEM

FIGURE 48-2. Inverted papilloma on an axial contrast-enhanced, T1-weighted, spin-echo MRI. The maxillary sinus is occupied by a solid mass that extends through an accessory ostium. The lesion exhibits a mixed pattern, which is typical.
### STAGING SYSTEM

#### Table 1. Krouse’s classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor restricted to the nasal cavity</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor restricted to the ethmoid sinus and medial/superior portion of the maxillary sinus</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor involving the lateral or inferior portions of the maxillary sinus or frontal or sphenoid sinuses</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor beyond nose and paranasal sinus boundaries or malignant disease</td>
</tr>
</tbody>
</table>

#### Tabela 1. Classificação de Krouse

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<tr>
<td>T1</td>
<td>Tumor limitado somente à cavidade nasal</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor limitado ao seio etmoidal e porções medial e superior do seio maxilar</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor envolve porções lateral ou inferior do maxilar ou seios frontal ou esfenoidal</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor além dos limites do nariz e seios paranasais ou doença maligna</td>
</tr>
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</table>
TREATMENT

- COMPLETE SURGICAL EXCISION.
- RECURRENCE CASES CAN BE DIFFICULT TO DIAGNOSE

SO !!
Squamous cell carcinoma antigen as a diagnostic marker of nasal inverted papilloma

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ABSTRACT

Objective: To clarify whether the level of serum SCCA can be used as a diagnostic marker of IP.

Methods: Serum SCCA level was measured in 30 patients with IP (IP group) and 57 with inflammatory disease (inflammatory group).

RESULTS: The serum SCCA levels in the IP group was significantly higher than those in the inflammatory group. The area under the curve was 0.888 (p<0.01). The sensitivity, specificity, positive predictive value, and negative predictive value of the serum SCCA level were 0.778, 0.844, 0.794, and 0.847, respectively. The results show that the serum SCCA level can be used as a diagnostic marker of IP.

CONCLUSION: The serum SCCA level can be used as a diagnostic marker of IP.

METHODS: A total of 20 patients with IP were enrolled and surgically treated from January 2010 to January 2013. A total of 15 patients with inflammatory disease were enrolled and surgically treated from January 2010 to January 2013.
METHODS

A total of 30 patients with IP in the paranasal sinus surgically treated from January 2006 to January 2015, took part in the present study (IP group). To investigate the significance of SCCA in the IP group, 57 patients with nasal and paranasal inflammatory diseases, such as chronic sinusitis, eosinophilic sinusitis, and postoperative maxillary cyst (inflammatory group), also participated in the present study. Surgical specimens from all the patients with IP and those with inflammatory disease were examined to confirm the pathology. Patients with pulmonary and skin diseases showed elevated serum SCCA levels; therefore, these diseases as well as smoking habit were recorded. The study protocol was approved by the institutional review board of the University of the Ryukyus. This study was conducted in accordance with the principles of the Declaration of Helsinki. Y. Yamashita and T. Uehara contributed equally to this study.
SCCA Measurement

Serum SCCA levels in the IP group were measured before and after surgery, and during the follow-up period. Patients in the inflammatory group were examined only before surgery. Because the elevated serum SCCA level in patients with oral cancer usually turned to normal within 4 days, the postoperative SCCA level was measured within 1 week after surgery. The SCCA level was measured by using the IMx SCCA microparticle enzyme immunoassay (Abbott Laboratories, Tokyo, Japan) until December 2009 and Architect, an automatic chemiluminescence immunoassay (Abbott Laboratories), from January 2009. Because the correlation coefficient of the SCCA level measured by the two different methods is 0.977, data obtained by using these two methods were considered identical. A level of ≤1.5 ng/mL was considered normal according to the manufacturers’ instructions.

Relationship between Clinical Characteristics and SCCA

The Krouse classification, history of previous surgery, recurrence after surgery, skin diseases, pulmonary function, smoking habit, and tumor volume were recorded retrospectively according to patients’ clinical records. Tumor volumes were measured by magnetic resonance imaging (MRI) by using the OsiriX Dicom Viewer 6.02 (Pixmeo, Geneva, Switzerland) software in the patients with IP.

SCCA Level Alteration in Recurrent Cases

The relationship between tumor volume and SCCA level alteration was determined in patients with recurrence after surgery.
RESULTS

Clinical Characteristics and Serum SCCA Level

The clinical characteristics of the patients with IP are shown in Table 1. The IP group consisted of 18 male and 12 female participants (age range, 10–77 years; median, 58.5 years), including 22 with new IP and 8 with recurrent IP who underwent previous surgery at another hospital. The mean and median observation periods after surgery were 36.6 months and 30.5 months, respectively.

Of 30 IP cases, 25 patients (83.3%) showed elevated serum SCCA levels, and 7 of 8 patients (87.5%) with recurrence also had elevated SCCA levels. There were no significant correlations between SCCA elevation and any of the observed clinical characteristics listed in Table 1 (sex, age, Krouse classification, previous surgery, recurrent case, respiratory function, and skin disease). Although the proportion of smokers in the high SCCA group was similar to the normal SCCA group, preoperative median SCCA values in smokers and never-smokers were 4.2 ng/mL (interquartile range, 1.9–8.4 ng/mL) and 2.0 ng/mL (interquartile range, 1.6–2.4 ng/mL), respectively. There was a significant difference in preoperative SCCA values between smokers and never-smokers ($p < 0.021$, Mann-Whitney $U$ test).
The inflammatory group consisted of 33 male and 24 female participants (age range, 10–78 years; median, 52.1 years), as shown in Table 2. There were only three patients (5.3%) with a high SCCA level in the inflammatory group. Of the three patients with an elevated SCCA level, two with a smoking history had mild pulmonary dysfunction and the one never-smoker had severe polyposis due to allergic fungal sinusitis. Among these three cases, two patients had normal SCCA levels after surgery. There was no significant correlation between SCCA elevation and clinical characteristics, including smoking status, in the inflammatory group (Table 2). Although the rate of never-smokers was smaller in the inflammatory group than in the IP group, the difference did not reach the level of significance.

The receiver operating characteristic curve analysis for SCCA level yielded an area under the curve of 0.889 (Fig. 1). Regarding the IP diagnosis in the IP and inflammatory groups based on the SCCA level (≤1.5 ng/mL), sensitivity, specificity, positive predictive value, negative predictive value, and predictive accuracy were 83.3, 94.7, 89.3, 91.5, and 90.8%, respectively.
Pre- and Postoperative SCCA Levels in the IP Group

The median preoperative serum SCCA level was 2.4 ng/mL (interquartile range, 1.7–5.2 ng/mL) in the IP group and 0.9 ng/mL (interquartile range, 0.6–1.3 ng/mL) in the inflammatory group. There was a significant difference in the preoperative SCCA concentration between the IP and inflammatory groups ($p < 0.001$) (Fig. 2). The median postoperative serum SCCA level in the IP group was 1.0 ng/mL (interquartile range, 0.8–1.4 ng/mL). In three patients, the SCCA level was $>1.5$ ng/mL within 1 week after surgery. There was a significant difference in SCCA levels between the pre- and postoperative stages in the IP group ($p < 0.001$) (Fig. 3).

Tumor Volume and SCCA Level

The mean (standard deviation) tumor volume measured by MRI was $14.1 \pm 8.9$ cm$^3$. The Spearman rank correlation analyses showed that the correlation coefficient of the preoperative SCCA level and tumor volume in the IP group was 0.522 ($p = 0.003$) (Fig. 4).
SCCA Level in Recurrent Cases

A total of 8 of 30 patients in the IP group received previous surgical treatment and had recurrent lesions. The pre- and postoperative median SCCA levels were 2.0 ng/mL (interquartile range, 1.6–3.0 ng/mL) and 0.9 ng/mL (interquartile range, 0.7–1.2 ng/mL), respectively. The postoperative SCCA concentration was significantly lower than in the preoperative value ($p = 0.017$) (Fig. 5).
Recurrent Cases after Surgery

Only 2 of 30 patients with IP (6.7%) had recurrent lesions after surgery. Both patients had elevated levels of SCCA at the time when the recurrent lesions were found. The clinical course of a representative patient with recurrent IP who received repeated measurements of SCCA levels for early detection of recurrence is shown in Fig. 6. The patient received lateral rhinotomy for removal of IP at another hospital. The preoperative SCCA level and the tumor volume were 8.6 ng/mL and 4.77 cm$^3$, respectively; the SCCA level decreased to 1.0 ng/mL after surgery. After the first operation at our hospital, the patient had three recurrences and received endoscopic surgical resections. The serum SCCA level increased at each recurrence, and, after surgery, the value returned to normal levels. Recurrent lesions could not be detected by MRI or computed tomography but could be detected by endoscopic examination and SCCA level in November 2001 and December 2012.
CONCLUSION

Serum SCCA is a diagnostic marker for distinguishing new and recurrent IP from inflammatory disease. Because the SCCA level was related to tumor volume, repeated SCCA level measurement after surgery combined with endoscopic, imaging, and pathologic examinations could detect small recurrent lesions. Although respiratory dysfunction and skin diseases were not related to the SCCA level in the present study, these conditions and smoking habit should be considered in the evaluation of the SCCA level.
Serum squamous cell carcinoma antigen is a useful biologic marker in patients with inverted papillomas of the sinonasal tract.

METHODS: The purpose of the current report was to study the expression of squamous cell carcinoma (SCC) antigen in sinonasal IPs and to evaluate the usefulness of SCC antigen as a biologic marker for the follow-up of patients with sinonasal IP. The expression of SCCA1 in three sinonasal IP cases, three sinonasal SCC cases, and cases of normal nasal epithelium were examined by Western blot analysis, and the SCCA1 expression pattern in sinonasal IPs and SCCa1 expression in IP specimens were evaluated immunohistochemically. The serum levels of SCC antigen in 10 patients with sinonasal IP and also were analyzed.

RESULTS: SCCA1 was overexpressed in all three sinonasal IP tissues compared with sinonasal SCC tissues or keratinocytes of all 31 sinonasal IP cases. In the four carcinoma in IP specimens, SCCA1 expression in the 10 of 11 patients with IP (91%) and significantly decreased after surgical resection of the tumors.

CONCLUSIONS: The results of the current study indicate that SCCA1 is frequently overexpressed and may play a biologic role in the development of sinonasal IPs. Serum SCC antigen may be a useful biologic marker in the follow-up of patients with sinonasal IP.

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ANY QUESTIONS?
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