



# Primary Intraosseous Carcinoma, Not Otherwise Specified with Ameloblastic Carcinoma Features in a Middle-aged Woman

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## ABSTRACT

Primary Intraosseous Carcinoma, Not Otherwise Specified (PIOC, NOS) is an extremely rare neoplasm defined as squamous cell carcinoma in the mandible, presumably from the residue of odontogenic epithelium. The diagnosis is often challenging, and the prognosis is poor. The treatment of choice is surgical excision but usually declined for cosmetic reasons. A 41-year-old Melanesian woman with a mass in her right jaw since two years ago but rapidly growing in the last six months, accompanied with pain. Irregular hard mass was found in the right mandible. Radiology studies revealed lytic tumors, likely infiltrating. No metastasis was found. The first biopsy revealed acanthomatous ameloblastoma, and the second biopsy revealed pseudoepitheliomatous hyperplasia. Wide excision was then conducted with pathology results of PIOC and NOS with some features of ameloblastic carcinoma. This case may arise from a previous benign precursor. Further genetic information may be needed. The treatment of choice is surgical excision. The prognosis needs further follow-up.

**Keywords:** Ameloblastic carcinoma, ameloblastoma, odontogenic, primary intraosseous carcinoma

## ABSTRAK

*Primary intraosseous carcinoma, not otherwise specified* (PIOC, NOS) merupakan keganasan odontogenik yang langka. Diagnosisnya sulit dengan prognosis buruk. Tata laksana utama adalah bedah eksisi yang cenderung ditolak karena alasan estetik. Seorang perempuan ras Melanesia usia 41 tahun, mengeluh benjolan rahang kanan sejak dua tahun dan makin membesar terutama 6 bulan terakhir disertai nyeri. Massa tidak teratur dengan batas tidak jelas di mandibula kanan dengan ukuran 10 x 8 x 4 cm. Pemeriksaan radiologis menegaskan massa infiltratif, tetapi tidak menemukan anak sebar. Biopsi awal menunjukkan ameloblastoma, biopsi selanjutnya menunjukkan *pseudoepitheliomatous hyperplasia*. Eksisi luas dilakukan dan patologi menemukan PIOC, NOS dengan sebagian ciri *ameloblastic carcinoma*. Patologi dari tiga biopsi menunjukkan massa jinak odontogenik yang mengalami inflamasi kronis kemudian menjadi ganas. Prognosis masih belum bisa dipastikan. **Stephen Utama Candinegara, Dewa Gede Subawa, Renaningtyas Tambun. Primary Intraosseous Carcinoma, Not Otherwise Specified dengan Gambaran Ameloblastik pada Perempuan Dewasa**

**Kata kunci:** Ameloblastoma, ameloblastic carcinoma, odontogenik, primary intraosseous carcinoma



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## BACKGROUND

Primary intraosseous carcinoma, not otherwise specified (PIOC, NOS) is an extremely rare neoplasm<sup>1</sup> defined as squamous cell carcinoma which develops in the mandible without any initial connection with the oral mucous membrane, adjoining skin or nasal or antral mucous membranes, presumably develops from the residue of odontogenic epithelium-derived embryologically from the dental ledge.<sup>2,3</sup> Diagnosis of PIOC and NOS is often challenging, as other lesions need to be excluded, such as metastasizing neoplasms to the jaws, gingival carcinomas that have invaded the bone, and neoplasms originating

from the maxillary sinus.<sup>4</sup> The 3-year survival rate of PIOC and NOS is 37%.<sup>5</sup> The treatment of choice is surgical excision, which usually declines for cosmetic reasons.<sup>6</sup>

Ameloblastoma is a rare neoplasm originating from odontogenic sources; its incidence rate is 0.5 cases per million populations.<sup>7</sup> It is a benign condition but locally infiltrative.<sup>8</sup> There are four pathological types of ameloblastoma. Acanthomatous ameloblastoma is a rare pathological feature of ameloblastoma that only occurs in 3,9 % of all ameloblastoma, generally in the age of 70s. This type of ameloblastoma is often falsely identified as

squamous cell carcinoma and is believed to be the most infiltrative type. Features of acanthomatous ameloblastoma are extensive squamous metaplasia, variable keratinization of stellate reticulum-like cells, and the formation of squamous edges in the center of the neoplastic nests, and calcification may be present. Histologically very similar to the squamous odontogenic tumor, but its peripheral cells are columnar instead of flat.<sup>9</sup> Ameloblastoma may tend to become malignant. PIOC, NOS is a rare malignancy from odontogenic precursors that may grow from benign ameloblastoma.<sup>10</sup> Ameloblastic carcinomas are tumors that combine

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morphologic features of ameloblastoma and carcinoma, regardless of metastasis. Ameloblastic carcinoma may arise as either primary malignant ameloblastoma that is not preceded by ordinary ameloblastoma (de novo carcinoma) or as a result of malignant change in pre-existing benign ameloblastoma (carcinoma ex ameloblastoma).<sup>11</sup>

### CASE

A 41-year-old Melanesian woman with a mass in her right jaw since two years ago but rapidly growing in the last six months with the pain while chewing foods. She lives in a rural area with difficult access to healthcare services and no history of malignancy from her family. On physical examination, we found an irregular hard mass in the right mandibular region, 10 x 8 cm in size, 4 cm highest, fixed to its base in the mandible. Some granulations with abscesses are found within the mass.



Figure 1. Clinical presentation of the mandibular mass.

The panoramic plain film revealed an extensive lytic tumor on the right mandible with a second molar tooth. MRI and CT scan revealed a mass in the right mandible, 5,4 x 4 x 5,6 cm in size, with hypointense characteristics in T1 and T2, relatively heterogenic, strongly enhanced after contrast was injected. The mass is poorly bordered with surrounding muscle, likely infiltrating the right mandible bone, causing bone cortex erosion with a second molar tooth—no metastasis was found in radiological examinations of the head, neck, chest, and abdomen.

Two incisional biopsies were conducted three

months apart. The first pathology result from the prior hospital revealed acanthomatous ameloblastoma. The patient was referred to our hospital for a second incisional biopsy. Histopathology of the second biopsy shows a well-matured hyperkeratotic epidermis

stromal infiltrated by dense acute and chronic inflammatory cells. The conclusion is pseudoepitheliomatous hyperplasia with active chronic inflammation, abscesses, and suspected focal invasive, but still cannot exclude acanthomatous ameloblastoma. Pus



Figure 2. Panoramic film.

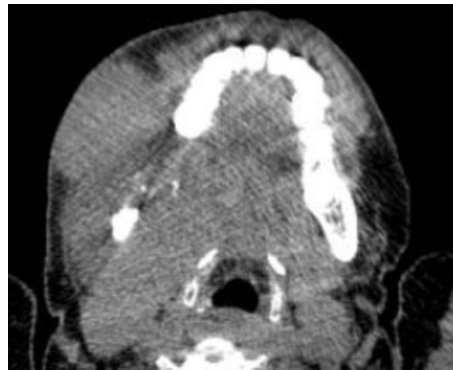


Figure 3. Axial CT scan of mandible.

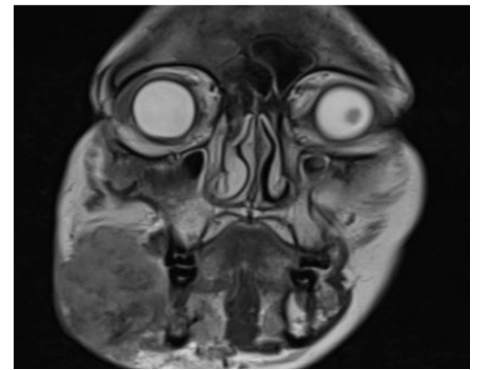


Figure 4. Coronal plane of head MRI.



Figure 5. Sagittal plane of head MRI



Figure 6. The tumor presentation intraoperatively.

with elongated rete ridges. Incomplete basal membrane found focally. Similar squamous cell islands and central necrosis are found separately in the dermal layer. Neither peripheral palisading, reverse polarization, nor stellate reticulum was identified. Fibrous

culture was also conducted with negative results.

Surgical wide excision was performed two weeks later. The mass was excised within the visible tumor margin, and a segmental



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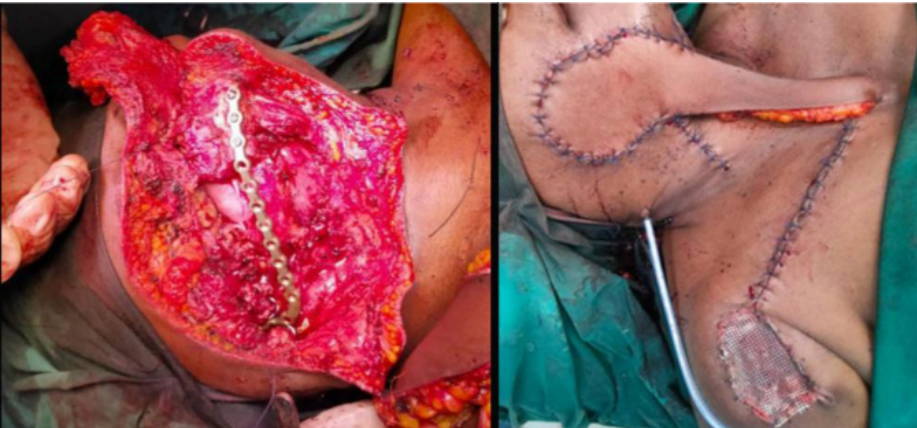


Figure 7. Surgical excision, internal fixation, and skin flap closure.

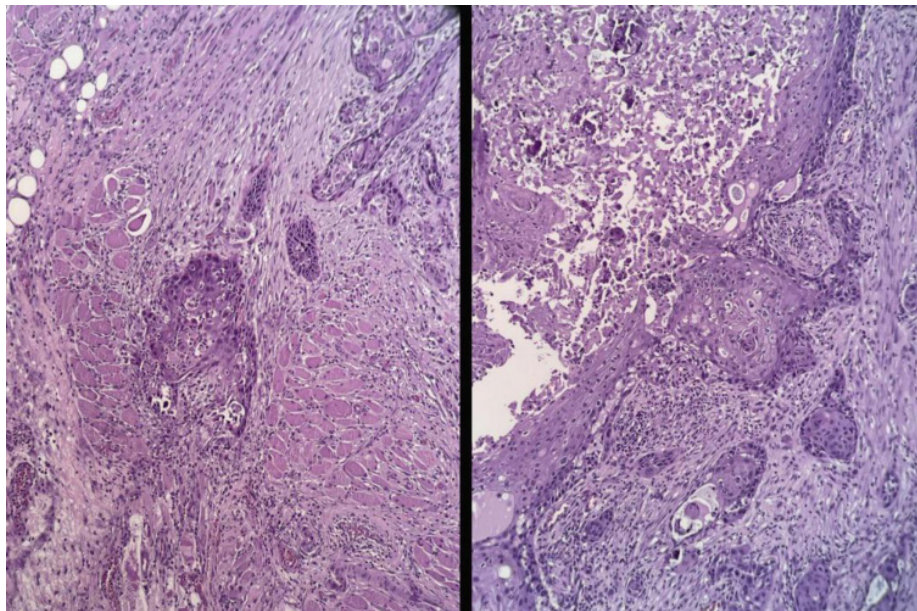


Figure 8. Pathology findings in 40x and 100x magnifications.

mandibulectomy was performed. Internal fixation of the mandible with plate and screw was done later. The regional flap from the right deltopectoral region was transferred to the recipient site on the right mandible. A split-thickness skin graft donor from the left hip was used to close the remaining unclosed flap donor. The tumor tissue and the right mandible bone were sent for pathology. After three weeks, the flap was closed. The patient is scheduled for radiotherapy.

Histopathology from the third surgical excision showed epithelial tumors invading the salivary gland, bone trabeculae, and skeletal muscles in a solid, trabecular, and cystic pattern generally with central keratinized pearl, keratinized mass, necrotic mass, and inflammatory cell infiltrate.

The nuclei are pleomorphic, bizarre, vesicular, hyperchromatic, conspicuous nucleoli, and glassy eosinophilic cytoplasm. Atypical mitosis is found. The stellate reticulum was impressed in some tumor islands without peripheral palisading or reverse polarity. The epidermis is ulcerative, hyperplastic, with elongated rete ridges. Fibrous stroma infiltrated by dense acute and chronic inflammatory cells. Perineural invasions were found. Surgical margins are not free from the tumor mass. PIOC and NOS were histopathologically confirmed, with ameloblastic and squamous cell carcinoma as differential diagnoses. As observed in Image 8, epithelial tumors were invading the salivary gland in a solid and trabecular pattern. Cystic pattern with central keratinized pearl, keratinized mass, necrotic

mass, and inflammatory cell infiltrate. The nuclei are pleomorphic, bizarre, vesicular, hyperchromatic, conspicuous nucleoli, and glassy eosinophilic cytoplasm.

### DISCUSSION

Odontogenic malignancies are classified into ameloblastic carcinoma, primary intraosseous carcinoma, NOS, sclerosing odontogenic carcinoma, clear cell odontogenic carcinoma, ghost cell odontogenic carcinoma, odontogenic carcinosarcoma, and odontogenic sarcoma. Any malignant epithelial tumor in the jaws is PIOC, NOS once the other differential diagnoses are ruled out. Commonly composed of moderately to poorly differentiated squamous epithelial cells with variable keratinization, PIOC and NOS arise from odontogenic epithelium with no precursor lesion or from odontogenic cyst epithelium or other benign precursors.<sup>1</sup>

Ameloblastic carcinoma has BRAF mutation similar to its benign condition, ameloblastoma. In addition to BRAF mutation, Ameloblastic carcinoma expresses SOX2 and has a higher Ki-67 proliferation index.<sup>1</sup> Ameloblastic carcinoma has classical features of ameloblastoma: peripheral palisading, reverse polarization, and stellate reticulum. Its features of malignancy include cytological atypia, pleomorphism with hyperchromasia, high N:C ratio, increased mitoses with atypical forms, and necrosis.<sup>7,12</sup>

In this patient, the first pathology is ameloblastoma. The pathology may change with the loss of some features of ameloblastoma, added with chronic inflammation signs, until signs of malignancies are found. The second biopsy revealed pseudoepitheliomatous hyperplasia, a benign hyperplastic epithelial condition composed of irregular elongated rete pegs extending deeply into the stroma. It typically occurs with chronic infections (tuberculosis, mycosis), trauma, and granular cell tumors classically. The cytological features of malignancy are not found in pseudoepitheliomatous hyperplasia.<sup>12</sup>

The third biopsy from surgical excision revealed epithelial tumors invading the salivary gland, bone trabeculae, and skeletal muscles with some of the ameloblastic carcinoma features. PIOC, NOS diagnosis was made.



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As the treatment of choice, wide surgical excision was conducted with the addition of segmental mandibulectomy and internal fixation. A positive tumor margin was found microscopically. Then radiotherapy is scheduled. Because of the positive tumor margin, it is essential to follow up

for tumor recurrence. Genetic information may be needed for further diagnosis to rule out ameloblastic carcinoma and other odontogenic malignancies.

### CONCLUSION

We reported a case of PIOC and NOS, with

some features of ameloblastic carcinoma. This case may arise from a previous benign odontogenic tumor, ameloblastoma. Further genetic information may be needed to confirm the diagnosis. The treatment of choice, in this case, is surgical excision of the tumor. The prognosis needs further follow-up.

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