Brunei International Medical Journal

OFFICIAL PUBLICATION OF
THE MINISTRY OF HEALTH
AND
UNIVERSITI BRUNEI DARUSSALAM

Volume 19 30 May 2023 (10 Zulkaedah 1444H)

ADENOSQUAMOUS CARCINOMA OF THE NASAL SEPTUM: A RARE VARIANT.

WONG Kim Yew Richard[1], Eyzawiah HASSAN[2], Azreen Zaira ABU BAKAR[3], Hafeza AHMAD[3], Shamim Rahman S.M.A ABDUL RASHEED[1], Asmawiza AWANG[3], Irfan MOHAMAD[4].

[1]Department of Otorhinolaryngology, Head & Neck Surgery, Kulliyah of Medicine, International Islamic University Malaysia, 25200 Kuantan, Pahang, Malaysia.
[2]Department of Otorhinolaryngology, Head & Neck Surgery, Faculty of Medicine & Health Sciences, Universiti Sains Islam Malaysia, 71800 Nilai, Negeri Sembilan, Malaysia.
[3]Department of Otorhinolaryngology, Head & Neck Surgery, Hospital Kuala Lumpur, 50586 Kuala Lumpur, Malaysia.
[4]Department of Otorhinolaryngology, Head & Neck Surgery, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, 16150 Kota Bharu, Kelantan, Malaysia.

ABSTRACT

Adenosquamous carcinoma is a rare variant of squamous cell carcinoma of the nasal septum which is very aggressive and metastasise early. We present a case of a gentleman who presented with left nasal septal swelling for 4 months. Examination showed a lesion at the left nasal septum extending to the dorsum of the nose and right upper lip region. Computed tomography scan of the paranasal sinuses and neck showed an enhancing lesion with ulceration at the left nasal septum, with regional metastasis to the neck. He underwent a subtotal rhinectomy, inferior maxillectomy, and bilateral modified radical neck dissection type III. Unfortunately, he succumbed to a cardiac arrest 5 days after surgery.

Keywords: Keywords: Adenosquamous carcinoma, Advance stage, Rhinectomy, Nasal septum, Squamous cell carcinoma.

Brunei Int Med J. *2023;19:13-18*

ISSN 1560 5876 Print
ISSN 2079 3146 Online

Online version of the journal is available at www.bimjonline.com

Brunei International Medical Journal (BIMJ)
Official Publication of
The Ministry of Health
and
Universiti Brunei Darussalam

EDITORIAL BOARD

Editor-in-Chief
Ketan PANDE

Sub-Editors
Vui Heng CHONG
William Chee Fui CHONG

Editorial Board Members
Muhd Syafiq ABDULLAH
Alice Moi Ling YONG
Ahmad Yazid ABDUL WAHAB
Jackson Chee Seng TAN
Pemasiri Upali TELISINGHE
Pengiran Khairol Asmee PENGIRAN SABTU
Dayangku Siti Nur Ashikin PENGIRAN TENGAH

INTERNATIONAL EDITORIAL BOARD MEMBERS

Lawrence HO Khek Yu (Singapore)
Wilfred PEH (Singapore)
Surinderpal S BIRRING (United Kingdom)
John YAP (United Kingdom)
Nazar LUQMAN (Australia)
Jose F LAPENA (Philippines)
Chuen Neng LEE (Singapore)
Emily Felicia Jan Ee SHEN (Singapore)
Leslie GOH (United Kingdom)
Ian BICKLE (United Kingdom)
Christopher HAYWARD (Australia)

Advisor
Wilfred PEH (Singapore)

Past Editors-in-Chief
Nagamuttu RAVINDRANATHAN
Kenneth Yuh Yen KOK
Chong Vui Heng
William Chong Chee Fui

Proof reader
John WOLSTENHOLME (CfBT Brunei Darussalam)

ISSN 1560-5876 Print
ISSN 2079-3146 Online

Aim and Scope of Brunei International Medical Journal

The Brunei International Medical Journal (BIMJ) is a six monthly peer reviewed official publication of the Ministry of Health under the auspices of the Clinical Research Unit, Ministry of Health, Brunei Darussalam.

The BIMJ publishes articles ranging from original research papers, review articles, medical practice papers, special reports, audits, case reports, images of interest, education and technical/innovation papers, editorials, commentaries and letters to the Editor. Topics of interest include all subjects that relate to clinical practice and research in all branches of medicine, basic and clinical including topics related to allied health care fields. The BIMJ welcomes manuscripts from contributors, but usually solicits reviews articles and special reports. Proposals for review papers can be sent to the Managing Editor directly. Please refer to the contact information of the Editorial Office.

Instruction to authors
Manuscript submissions
All manuscripts should be sent to the Managing Editor, BIMJ, Ministry of Health, Brunei Darussalam; e-mail: editor-in-chief@bimjonline.com. Subsequent correspondence between the BIMJ and authors will, as far as possible via should be conducted via email quoting the reference number.

Conditions
Submission of an article for consideration for publication implies the transfer of the copyright from the authors to the BIMJ upon acceptance. The final decision of acceptance rests with the Editor-in-Chief. All accepted papers become the permanent property of the BIMJ and may not be published elsewhere without written permission from the BIMJ.

Ethics
Ethical considerations will be taken into account in the assessment of papers that have experimental investigations of human or animal subjects. Authors should state clearly in the Materials and Methods section of the manuscript that institutional review board has approved the project. Those investigators without such review boards should ensure that the principles outlined in the Declaration of Helsinki have been followed.

Manuscript categories
Original articles
These include controlled trials, interventional studies, studies of screening and diagnostic tests, outcome studies, cost-effectiveness analyses, and large-scale epidemiological studies. Manuscript should include the following; introduction, materials and methods, results and conclusion. The objective should be stated clearly in the introduction. The text should not exceed 2500 words and references not more than 30.

Review articles

These are, in general, invited papers, but unsolicited reviews, if of good quality, may be considered. Reviews are systematic critical assessments of literature and data sources pertaining to clinical topics, emphasising factors such as cause, diagnosis, prognosis, therapy, or prevention. Reviews should be made relevant to our local setting and preferably supported by local data. The text should not exceed 3000 words and references not more than 40.

Special Reports

This section usually consist of invited reports that have significant impact on healthcare practice and usually cover disease outbreaks, management guidelines or policy statement paper.

Audits

Audits of relevant topics generally follow the same format as original article and the text should not exceed 1,500 words and references not more than 20.

Case reports

Case reports should highlight interesting rare cases or provide good learning points. The text should not exceed 1000 words; the number of tables, figures, or both should not be more than two, and references should not be more than 15.

Education section

This section includes papers (i.e. how to interpret ECG or chest radiography) with particular aim of broadening knowledge or serve as revision materials. Papers will usually be invited but well written paper on relevant topics may be accepted. The text should not exceed 1500 words and should include not more than 15 figures illustration and references

three relevant references should be included. Only images of high quality (at least 300dpi) will be acceptable.

Technical innovations

This section include papers looking at novel or new techniques that have been developed or introduced to the local setting. The text should not exceed 1000 words and should include not more than 10 figures illustration and references should not be more than 10.

Letters to the Editor

Letters discussing a recent article published in the BIMJ are welcome and should be sent to the Editorial Office by e-mail. The text should not exceed 250 words; have no more than one figure or table, and five references.

Criteria for manuscripts

Manuscripts submitted to the BIMJ should meet the following criteria: the content is original; the writing is clear; the study methods are appropriate; the data are valid; the conclusions are reasonable and supported by the data; the information is important; and the topic has general medical interest. Manuscripts will be accepted only if both their contents and style meet the standards required by the BIMJ.

Authorship information

Designate one corresponding author and provide a complete address, telephone and fax numbers, and e-mail address. The number of authors of each paper should not be more than twelve; a greater number requires justification. Authors may add a publishable footnote explaining order of authorship.

Group authorship

If authorship is attributed to a group (either solely or in addition to one or more individual authors), all members of the group must meet the full criteria and requirements for authorship described in the following paragraphs. One or more authors may take responsibility 'for' a group, in which case the other group members are not authors, but may be listed in an acknowledgement.

Authorship requirement

sign, and the analysis and interpretation of the data (where applicable); to have made substantial contributions to the writing or revision of the manuscript; and to have reviewed the final version of the submitted manuscript and approved it for publication. Authors will be asked to certify that their contribution represents valid work and that neither the manuscript nor one with substantially similar content under their authorship has been published or is being considered for publication elsewhere, except as described in an attachment. If requested, authors shall provide the data on which the manuscript is based for examination by the editors or their assignees.

Financial disclosure or conflict of interest

Any affiliation with or involvement in any organisation or entity with a direct financial interest in the subject matter or materials discussed in the manuscript should be disclosed in an attachment. Any financial or material support should be identified in the manuscript.

Copyright transfer

In consideration of the action of the BIMJ in reviewing and editing a submission, the author/s will transfer, assign, or otherwise convey all copyright ownership to the Clinical Research Unit, RIPAS Hospital, Ministry of Health in the event that such work is published by the BIMJ.

Acknowledgements

Only persons who have made substantial contributions but who do not fulfill the authorship criteria should be acknowledged.

Accepted manuscripts

Authors will be informed of acceptances and accepted manuscripts will be sent for copyediting. During copyediting, there may be some changes made to accommodate the style of journal format. Attempts will be made to ensure that the overall meaning of the texts are not altered. Authors will be informed by email of the estimated time of publication. Authors may be requested to provide raw data, especially those presented in graph such as bar charts or figures so that presentations can be constructed following the format and style of the journal. Proofs will be sent to authors to check for any mistakes made

DISCLAIMER

All articles published, including editorials and letters, represent the opinion of the contributors and do not reflect the official view or policy of the Clinical Research Unit, the Ministry of Health or the institutions with which the contributors are affiliated to unless this is clearly stated. The appearance of advertisement does not necessarily constitute endorsement by the Clinical Research Unit or Ministry of Health, Brunei Darussalam. Furthermore, the publisher cannot accept responsibility for the correctness or accuracy of the advertisers' text and/or claim or any opinion expressed.

ADENOSQUAMOUS CARCINOMA OF THE NASAL SEPTUM: A RARE VARIANT.

WONG Kim Yew Richard[1], Eyzawiah HASSAN[2], Azreen Zaira ABU BAKAR[3], Hafeza AHMAD[3], Shamim Rahman S.M.A ABDUL RASHEED[1], Asmawiza AWANG[3], Irfan MOHAMAD[4].

[1]Department of Otorhinolaryngology, Head & Neck Surgery, Kulliyah of Medicine, International Islamic University Malaysia, 25200 Kuantan, Pahang, Malaysia.
[2]Department of Otorhinolaryngology, Head & Neck Surgery, Faculty of Medicine & Health Sciences, Universiti Sains Islam Malaysia, 71800 Nilai, Negeri Sembilan, Malaysia.
[3]Department of Otorhinolaryngology, Head & Neck Surgery, Hospital Kuala Lumpur, 50586 Kuala Lumpur, Malaysia.
[4]Department of Otorhinolaryngology, Head & Neck Surgery, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, 16150 Kota Bharu, Kelantan, Malaysia.

ABSTRACT

Adenosquamous carcinoma is a rare variant of squamous cell carcinoma of the nasal septum which is very aggressive and metastasise early with poor prognosis. We present a case of a gentleman who presented with left nasal septal swelling for 4 months. Examination showed a lesion at the left nasal septum extending to the dorsum of the nose and right upper lip region. Computed tomography scan of the paranasal sinuses and neck showed an enhancing lesion with ulceration at the left nasal septum, with regional metastasis to the neck. He underwent a subtotal rhinectomy, inferior maxillectomy, and bilateral modified radical neck dissection type III. Unfortunately, he succumbed to a cardiac arrest 5 days after surgery.

Keywords: Adenosquamous carcinoma, Advance stage, Rhinectomy, Nasal septum, Squamous cell carcinoma.

INTRODUCTION

Malignancy of the nasal septum are infrequently encountered, and it comprises less than 10% of sinonasal malignancies.[1] The most common type of malignancy is the squamous cell carcinoma. The adenosquamous variant of the squamous cell carcinoma is very rare. Only about a hundred cases in the head and neck region are reported so far in literature. When present, it is known to be extremely aggressive and shows very rapid local and distant spread with poor prognosis.[2] We present a case of a 72-year old gentleman who presented with a nasal septal adenosquamous carcinoma, stage IVA (T4a N2c M0), who underwent a subtotal rhinectomy, inferior maxillectomy, and bilateral modified radical neck dissection type III, but succumbed to a cardiac arrest 5 days after surgery.

Corresponding author: Eyzawiah HASSAN, Department of Otorhinolaryngology, Head & Neck Surgery, Faculty of Medicine & Health Sciences, Universiti Sains Islam Malaysia, 71800 Nilai, Negeri Sembilan, Malaysia.
Tel: +60199101179; email: eyzawiah@usim.edu.my.

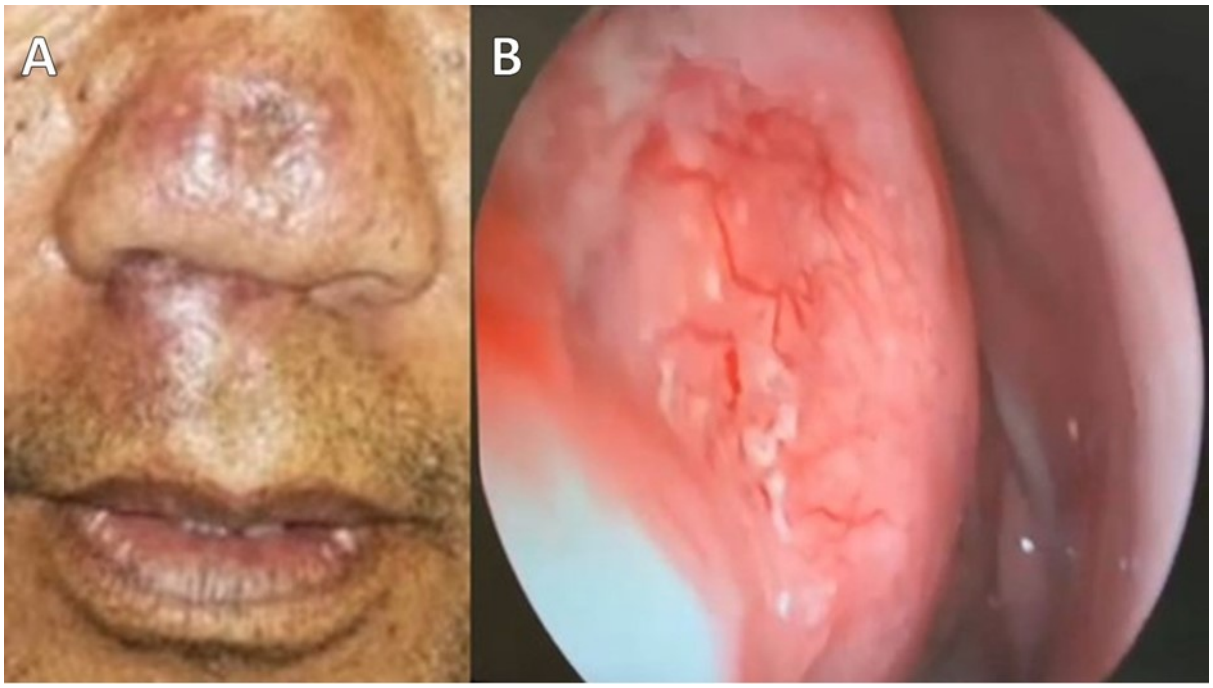

Figure 1: (A) Lesion at the dorsum of the nose with central ulceration (yellow arrow). (B) Nasoendoscopy showing a left septal mass with visible vessels on its surface (red arrow).

CASE REPORT

A 72-year-old Malay gentleman, with underlying diabetes mellitus, hypertension and ischaemic heart disease, presented with history of progressive left-sided nasal blockage for 4 months. It was associated with nasal pain, swelling and left blood-stained nasal discharge. Otherwise, there was no associated history of foul smelly rhinorrhea, headache, visual impairment, hyposmia, epiphora, facial numbness or neck swelling. He was a non-smoker, however, he worked as a farmer with prolonged exposure to pesticides.

Examination of the nose showed nasal tip depression, and a lesion at the dorsum of the nose measuring 2 x 2 cm with central ulceration (Figure 1A). Anterior rhinoscopy revealed a mass extending from the left nasal septum to the columella and the right upper lip region. It was firm-to-hard in consistency, erythematous and was tender on palpation. Nasoendoscopy showed a mass at the left nasal septum about 2 x 2cm, extending superiorly to the roof of the nasal septum, inferiorly to the floor of nasal cavity, and posteriorly to posterior half of the septum (Figure 1B). Otherwise, the bilateral inferior turbinates, osteomeatal complexes, nasopharynx and Fossa of Rosenmuller were normal. Intraoral examination showed normal hard and soft palates and oropharynx. Upon examination of the neck, there was a painless palpable 2x1cm neck lymphadenopathy at right level Ib.

Radiological assessment via contrast-enhanced computed tomography (CECT) scan of the nose and paranasal sinuses revealed an enhancing soft tissue lesion at the left side of the cartilaginous nasal septum, measuring 4.4 x 2.7 x 4.7cm (AP x W x CC) (Figure 2). There was involvement of external nasal cartilages, the subcutaneous tissue and the skin of the nose, with partial encasement of bilateral nostrils. Posteriorly, there was encasement and erosion of the anterior part of the bony nasal septum. Superiorly, the lesion abuts the nasal bone with bony erosion demonstrated. Inferiorly, there was erosion of the anterior cortex of the hard palate. Antero-inferiorly, it involved the philtrum and encroached the upper lip with no clear fat plane demonstrated.

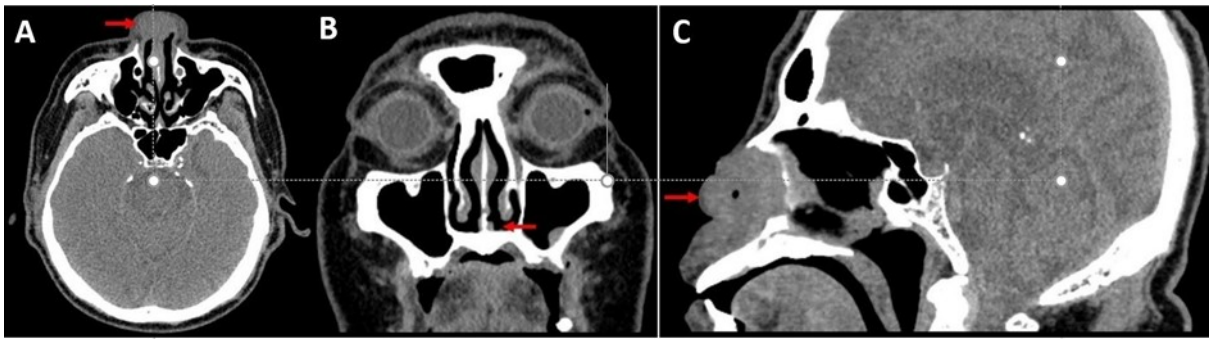

Figure 2: Axial (A), coronal (B) and sagittal (C) views of CECT scan of the nose and paranasal sinuses showing the enhancing soft tissue lesion (red arrows) at the left side of the cartilaginous nasal septum. (Click on image to enlarge)

There were enlarged bilateral level Ib lymph nodes, measuring 1.2cm in largest diameter, with subcentimeter level II and III nodes, clinically Stage IVA (T4a N2c M0). Otherwise, there were no distant metastases noted on CECT scan of the thorax, abdomen, pelvis and bony structures.

Multiple biospsies of the left nasal mass revealed multiple fragments of tumour tissue partly covered by stratified squamous epithelium with intermingling respiratory type epithelium. These features favoured the clinical diagnosis of a nasal septal adenosquamous carcinoma. The patient was consented and underwent a subtotal rhinectomy, inferior left maxillectomy, bilateral modified radical neck dissection type III and local upper lip advancement flap. Unfortunately, the patient succumbed to a cardiac event 5 days post-surgery.

Histopathological examination of the resected specimen showed a tumour tissue covered partly by stratified squamous epithelium and partly by respiratory-type columnar epithelium, with presence of adnexal structures of sebaceous glands and hair follicles (Figure 3). These tissues were infiltrated by malignant cells arranged in irregular clusters and many forming central lumen or glandular structures. The cells in tight irregular clusters showed squamoid differentiation with polygonal shape and dense eosinophilic cytoplasm and individual keratinization. The surrounding stroma showed desmoplastic reaction which was heavily infiltrated by plasmolymphocytic cells, and presence of seromucinous glands. The neoplastic cells exhibit moderate nuclear pleomorphism, mitosis, vesicular nuclei and prominent nucleoli. Immunohistochemistry studies showed the neoplastic cells were positive for p40, p16, CK 5/6, CK7, EMA and CEA (Figure 4 and 5). The superior, inferior and left lateral margins were involved by the tumour, however, other margins were clear. No malignancy was seen in all the lymph nodes dissected.

DISCUSSION

Adenosquamous carcinoma (ASC) is a rare variant of squamous cell carcinoma (SCC), and the WHO has defined it as a malignant tumour with mixed differentiation of both SCC and true adenocarcinoma, with both components occurring in close proximity but distinct

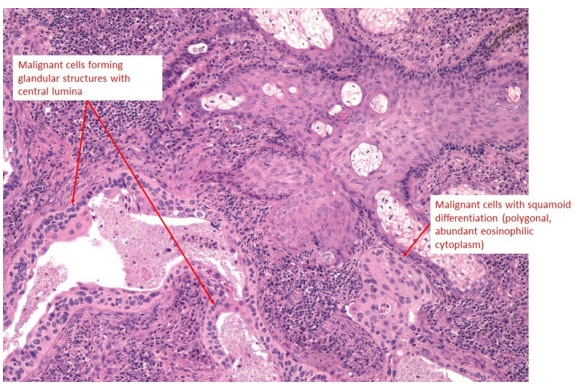

Figure 3: Histopathological findings of tumour tissue with both stratified squamous and respiratory-type columnar epithelium differentiation. (Click on image to enlarge)

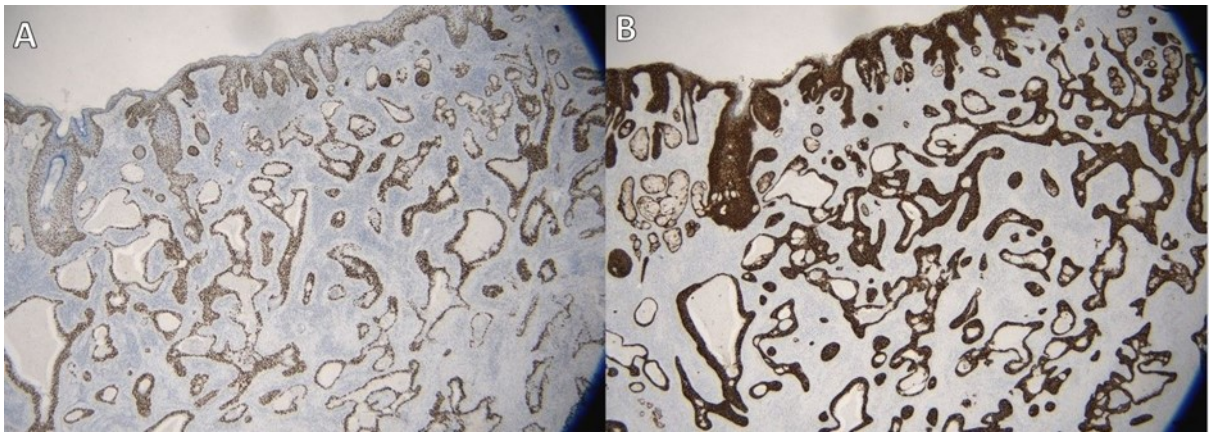

Figure 4: Immunohistochemistry studies show the neoplastic cells are positive for p40 (A) and CK5/6 (B) showing the squamous component of the tumour.

from one another. Gerughty et al in 1968 first described it as a type of malignant salivary gland tumor.[2] The most common sites of occurrence of this malignancy are at the head and neck region, and the subsites that are frequently involved include larynx (48.4%), followed by the oral cavity (30%). The nose and paranasal sinuses are rare sites for occurrence of this tumour, making the present case a unique and interesting one. To date, only 7 cases have been reported in literature.[3] It has a predilection among the male population with a male to female ratio of between 9:1 and 2:1. The median age of occurrence is about 60 years.[4] Risk factors for these tumours include cigarette smoking and exposure to wood dust, nickel, and chemical solvents.[5] In our case, the prolonged exposure to chemical solvents in pesticides may be a risk factor.

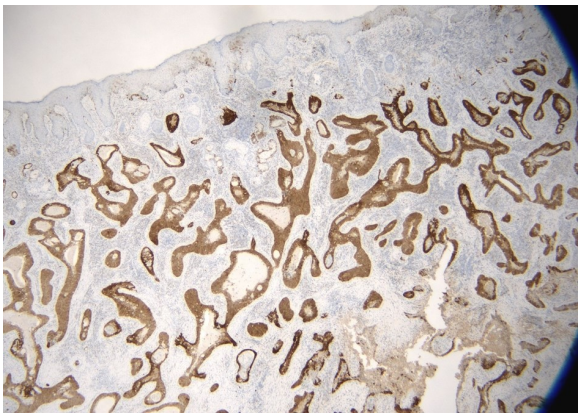

Figure 5: Immunohistochemistry studies show the neoplastic cells are positive for p16, which is a surrogate marker for *Human papillomavirus* infection. (Click on image to enlarge)

Histologically, diagnosis of ASC requires two distinct components. Squamous cell carcinoma is usually the predominant subtype, which may be well or poorly differentiated. The squamous epithelium is characterized by two or more of the following features, which are; intercellular bridging, formation of keratin pearls, parakeratotic differentiation, individual cell keratinisation and cellular arrangements which show pavement or mosaic pattern. The adenocarcinomatous component may show a tubular, alveolar and/or glandular morphology. The gland formation, predominantly in the deepest neoplastic areas, classically consists of 'punched out' spaces with smooth edges. Mucin production is typically present. The glandular epithelium shows characteristic demonstration of intracytoplasmic or intraductal sialomucin by high iron diamine (alcian blue or periodic acid–Schiff stain retention after diastase digestion) and Mayer's mucicarmine. [6] These tumours always have infiltrating margins, usually with solid small tumour nests or thin trabeculae in a desmoplastic stroma, as is noted in our case.

Among the differential diagnoses of ASC are salivary gland mucoepidermoid carci-

noma (MEC) and acantholytic and basaloid squamous cell carcinoma. MEC are composed predominantly of intermediate or epidermoid cells but without keratin formation. MEC usually has a lobular pattern and infiltrates forming wide sheets of neoplastic cells with round contours; but lacks the severe dysplasia or carcinoma in situ component that is found in ASC. It is crucial to differentiate between these two entities as ASC is a very aggressive tumour with a worse prognosis than high-grade MEC. To differentiate from SCC, besides the presence of mucin production; immunohistochemical staining of ASC shows positivity for CEA (92%), CK7 (75%) and CAM 5.2 (58%), while SCC, though positive for CK 5/6 and p40; is either negative or focally reactive for these markers. The high molecular weight cytokeratin 34BE12 is positive in both ASC and SCC.[7]

Nasal obstruction is the commonest symptom at presentation, followed by epistaxis. In patients with more advanced diseases, they may present with nasal swelling, epiphora, diplopia, proptosis, or palatal ulceration. Upon examination, a nasal mass is the most common finding, followed by nasal septal ulcers. Endoscopic nasal examination is useful to aid in the diagnosis. Definitive diagnosis is made by histopathological examination.[8] CECT and magnetic resonance imaging are useful to evaluate the extent and the characteristics of the tumour. Pre-operatively, they are helpful to rule out anatomical variations and assist in surgical planning.

Treatment includes surgery, radiation therapy or combined therapies. Surgical resection with one centimeter margins and the removal of full thickness mucosa, cartilage and/or bone is the preferred choice of treatment modality as the septum is easily accessible.[1] Some smaller lesions could be completely excised with wide local resection and frozen sections. In some early-stage diseases, endoscopic resection provides good tumour control and is cosmetically favourable.[3,8]

Treatment includes surgery, radiation therapy or combined therapies. Surgical resection with one centimeter margins and the removal of full thickness mucosa, cartilage and/or bone is the preferred choice of treatment modality as the septum is easily accessible.[1] Some smaller lesions could be completely excised with wide local resection and frozen sections. In some early-stage diseases, endoscopic resection provides good tumour control and is cosmetically favourable.[3,8]

Rhinectomy is indicated if the anterior nasal bone is involved, and in large anterosuperior nasal septum malignancies.[9] Postoperative radiotherapy is required in large tumours (AJCC Stage T3 or greater), tumours in which one-centimeter clear resection margin is not achieved, tumours which involved critical regions like the anterior skull base and orbit; tumours with lymph node metastasis, and recurrent disease.[10] Reconstruction is offered after all tumour treatment is completed to avoid compromising tumour treatment.[11]

Only small accessible lesions of the nasal septum are treated primarily by radiotherapy as a single modality of treatment. However, radiotherapy is not indicated in superior nasal septum tumours due to the proximity of the optic chiasm. Side effects of radiotherapy such as chronic nasal pain, periorbital swelling and blindness have been reported. Systemic therapy is not routinely used in managing these tumours.[12]

Overall, these tumours are extremely aggressive and highly malignant. Some of these tumours harbour *Human papillomavirus* and show overexpression of p16. However, unlike oropharyngeal cancers that are HPV-related, this does not seem to be a good marker of prognosis. [13] Therefore, should our case survive the initial surgery, he should be planned for adjuvant radiotherapy as well.

ASC have a high propensity to recur. 47% of patients developed local recurrence, while 65% developed nodal metastasis and 23% experienced distant metastasis, with a 5 -year survival rate of 13%. Therefore, early and frequent follow-up is vital.[14]

CONCLUSION

Adenosquamous carcinoma of the nasal septum is an extremely rare tumour that histologically incorporates both squamous cell carcinoma and adenocarcinomatous morphology. It is known to be locally aggressive and highly malignant. Early detection, with surgery and radiotherapy offers the best hope for long term survival.

ACKNOWLEDGEMENT

Authors' contribution: WKYR, AZAB, NEH and SRSAR contributed to the concept, design and drafting of the manuscript. WKYR, AZAB, EK and HA were involved in clinical and surgical management of the patient. WKYR and AZAB contributed to obtaining the clinical and radiological images. AA contributed to providing the histopathological examination report and microscopic pictures. IM provided the academic input. All authors revised and approved the final manuscript.

Special thanks to the Director General of Health, Ministry of Health, Malaysia for the permission to publish this case report.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1: Lee DH, Lim SC, Yoon SH, Kang TG, Park JM. Clinical analysis of benign and malignant nasal septal tumors. Korean Journal of Otorhinolaryngology-Head and Neck Surgery. 2019; 62 (4): 228–232.

2: Gerughty RM, Hennigar GR, Brown FM. Adenosquamous carcinoma of the nasal, oral and laryngeal cavities. A clinicopathologic survey of ten cases. Cancer. 1968; 22: 1140–1155.

3: Shinhar SY, Heckathorn CL. Adenosquamous carcinoma of the nasal cavity. Ear, Nose & Throat Journal. 2008; 87(11): 612–614.

4: Benat G, Cros A, Sarini J, Galissier T, Collins F, Laurencin-Dalicieux S, et al. Adenosquamous carcinoma, a rare and unknown tumor. Journal of Oral Medicine and Oral Surgery. 2018; 24 (3): 133–137.

5: Bhattacharyya N. Cancer of the nasal cavity. Archives of Otolaryngology–Head & Neck Surgery. 2002; 128(9): 1079-1083.

6: Thanakappan P, Venkata NS, Amudala R, Botu M. Adenosquamous carcinoma of oral cavity. Journal of Cancer Research and Therapeutics. 2015; 11(4): 1034.

7: Alos L, Castillo M, Nadal A, Caballero M, Mallofre C, Palacin A, et al. Adenosquamous carcinoma of the head and neck: criteria for diagnosis in a study of 12 cases. Histopathology. 2004; 44(6): 570–579.

8: Çukurova İ. Squamous cell carcinoma originating from the nasal septal perforation: a rare nasal tumor. The Turkish Journal of Ear Nose and Throat. 2014; 24(3): 177–180.

9: Ho YM, Coman WB. Nasal septum malignancy. ANZ Journal of Surgery. 2011; 81(7-8): 533–536.

10: Miyazaki T, Haku Y, Yoshizawa A, Iwanaga K, Fujiwara T, Mizuta M, et al. Clinical features of nasal and sinonasal inverted papilloma associated with malignancy. Auris Nasus Larynx. 2018; 45(5): 1014-1019.

11: Ethunandan M, Downie I, Flood T. Implant-retained nasal prosthesis for reconstruction of large rhinectomy defects: the Salisbury experience. International Journal of Oral and Maxillofacial Surgery. 2010; 39(4): 343–349.

12: Allen MW, Schwartz DL, Rana V, Adapala P, Morrison WH, Hanna EY, et al. Long-term radiotherapy outcomes for nasal cavity and septal cancers. International Journal of Radiation Oncology, Biology and Physics. 2008; 71(2): 401–406.

13: Masand RP, El-Mofty SK, Ma X-J, Luo Y, Flanagan JJ, Lewis JS. Adenosquamous carcinoma of the head and neck: relationship to human papillomavirus and review of the literature. Head and Neck Pathology. 2011; 5(2): 108–116.

14: Keelawat S, Liu CZ, Roehm PC, Barnes L. Adenosquamous carcinoma of the upper aerodigestive tract: A clinicopathologic study of 12 cases and review of the literature. American Journal of Otolaryngology. 2002; 23: 160-168.