Hawai‘i Journal of Health & Social Welfare
A Journal of Pacific Health & Social Welfare

September 2023, Volume 82, No. 9, ISSN 2641-5216

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Mediastinal Epithelioid Angiosarcoma, New Insights into an Uncommon Diagnosis: A Case Report and Literature Review

Janira M. Navarro Sanchez MD; Tiffany Oommen DO; Christopher Lum MD; Zan Halford MS, MB (ASCP); and Koah Vierkoetter MD

Abstract

Angiosarcoma is an uncommon malignant mesenchymal neoplasm, accounting for 1–2% of all sarcomas. More than half are cutaneous, with the remainder arising in the deep soft tissue, breast, bone or viscera, particularly the liver, spleen and heart. Mediastinal angiosarcomas are exceedingly uncommon. While epithelioid morphology is sometimes a minor component in conventional angiosarcoma, tumors with a predominance of epithelioid morphologic features are designated as epithelioid angiosarcoma (EAS). This is a report of a 58-year-old woman presenting with severe chest pain, accompanied by worsening dyspnea and dysphagia. Chest computed tomography (CT) revealed a large pericardial effusion and a bulky mediastinal mass. Biopsy revealed a malignant neoplasm with vascular differentiation consistent with high-grade EAS. By immunohistochemistry, epithelioid angiosarcomas express endothelial cell markers, such as CD31, CD34, ERG and FLI-1. A variable proportion express low molecular weight cytokeratin (CK), epithelial membrane antigen (EMA) and CD30. The use of molecular techniques has proven useful in the diagnosis of this rare neoplasm. Targeted next generation sequencing showed aberrations in multiple genes including NRAS, KRAS, MYC and TP53.

Keywords

Angiosarcoma, Epithelioid Angiosarcoma, Mediastinum, Sarcoma

Abbreviations and Acronyms

CK = cytokeratin
CNB = core needle biopsy
CT = chest computed tomography
EAS = epithelioid angiosarcoma
EHE = epithelioid hemangioendothelioma
EMA = epithelial membrane antigen
ERG = immunohistochemical stain, member of the ETS family of transcription factors, highly specific endothelial marker
FNA = fine needle aspiration
NGS = next generation sequencing
TMB = tumor mutation burden

Introduction

Angiosarcoma is a rare malignant vascular neoplasm, which originates from the endothelial cells of blood vessels. They may arise in any part of the body and affect any organ.1 The peak age of incidence is the 7th decade, with men affected more than women. The head and neck area is the most common site of diagnosis for primary angiosarcoma. Radiation-induced angiosarcoma most commonly occurs in the breast.2

Epithelioid vascular tumors encompass a spectrum of disease that includes epithelioid hemangioma (EH; a benign neoplasm), epithelioid hemangioendothelioma (EHE; a low to intermediate grade malignancy) and epithelioid angiosarcoma (EAS; a high-grade malignancy).3

Histologically, epithelioid vascular tumors may appear similar with diagnostic challenges at the malignant end of the spectrum (ie, high grade EHE vs high-grade EAS). This distinction is aided by molecular analysis, as approximately 90% of EHE with classic morphology harbor a t(1;3) (p36; q23-25) translocation resulting in a fusion of WWTR1 (3q23-24) with CAMTA1 (1p36). This gene fusion has not been identified in other vascular tumors, and diffuse nuclear immunoreactivity for CAMTA1 protein has been reported in the majority of conventional EHE.3

The differential diagnosis includes nonvascular lesions with epithelioid morphology, including melanoma, carcinoma, and other epithelioid soft tissue tumors.

Described here is a rare case of mediastinal EAS. Targeted next generation sequencing (NGS) was performed in this case. To the authors’ knowledge, this is the first case report of this entity in the mediastinum that includes molecular findings.

Case Presentation: Clinical History and Pathology Findings

The patient is a 58-year-old female with a significant smoking history who presented with acute onset severe, non-radiating left sided chest pain along with 1 month of worsening dyspnea and dysphagia. Chest computed tomography (CT) revealed a large pericardial effusion, non-specific periportal liver edema, small left pleural effusion, and a bulky mediastinal mass. Due to concern for impending tamponade, she underwent emergent pericardiocentesis with removal of 650 mL of serosanguineous fluid and subsequent resolution of symptoms. Initial cytology/cell block from pericardial fluid showed tumor cells with an epithelioid/plasmacytoid appearance and abundant dense cytoplasm. The tumor nuclei were large, atypical, with prominent nucleioli and multinucleated forms (Figure 1 a-b). Immunostains on the cellblock demonstrated an absence of differentiation of the tumoral cells (cytokeratin AE1/AE3, cytokeratin 7, cytokeratin 8/18, LCA, CD30, CD15, PAX-5, calretinin, TTF-1, Napsin-A, S100, SALL4 and OCT3/4).
A CT-guided core needle biopsy (CNB) of the anterior mediastinal mass was recommended. Mediastinal mass CNB showed atypical cells in a background of lymphocytes. The cells were weakly immunopositive for epithelial membrane antigen (EMA) and negative for other markers (cytokeratin AE1/AE3, cytokeratin 8/18, cytokeratin 5/6, high molecular weight cytokeratin (HMWCK), cytokeratin 7, cytokeratin 20, PAX8, TTF1, WT1, p40, GATA3, CD45, CD5, CD30, CD138, ALK1, TdT, CD43, CD34, PAX5, MUM1, SOX10, MelanA, S100, SALL4, OCT3/4). Flow cytometry was negative for a clonal B or abnormal T-cell population. Due to the non-specific EMA positivity, which can be seen in carcinomas, subsets of hematolymphoid, mesothelial and sarcomatous neoplasias, a diagnosis of poorly differentiated malignant neoplasm was rendered, with request of additional tissue for further characterization.

The patient was subsequently admitted with reoccurrence of symptoms and imaging suggestive of persistent pericardial effusion. Repeat pericardiocentesis was performed for rapid fluid accumulation. A left video-assisted thoracotomy with conversion to left thoracotomy was performed, with placement of a pericardial window, and biopsy of the mediastinal mass. The largest fragment of the surgical specimen measured 2.5 x 2.0 x 0.7 cm. Hematoxylin and eosin stained slides showed sheets of epithelioid cells with scattered markedly pleomorphic forms. The tumoral cells exhibited abundant eosinophilic cytoplasm with occasional intracytoplasmic vacuoles. Nuclei were large and atypical with prominent nucleoli. Mitotic figures and necrosis were present throughout (Figure 2 a-d). Immunostains were positive for vimentin, CD31, ERG (immunohistochemical stain, member of the ETS family of transcription factors, highly specific endothelial marker) (Figure 3 a-b), TLE1, CD99 and h-caldesmon. There was weak staining for EMA. Immunostains for CD34, STAT6, cytokeratin AE1/AE3, CK8/18, calretinin, SMA, desmin, CD68, CD117, HHV8 and PLAP were negative. Given the immunohistochemical evidence of vascular differentiation, the differential diagnosis included EHE and EAS, amongst others. CAMTA1 immunohistochemistry was negative. With the exclusion of EHE, the final diagnosis was high grade EAS.

Given the patient’s diagnosis of stage IV EAS, palliative radiotherapy was recommended; however, considering the poor prognosis and estimated survival of less than 6 months, the patient declined therapy and elected to pursue hospice services.

**Molecular Findings**

Targeted next generation sequencing (NGS) detected a missense NRAS mutation c.182A>G(p.Gln61Arg) and a splice donor site in TP53 c.375+2T>A. Amplification of AKT2, ATM, BRAF, CCND1, CDK6, CHEK1, EGFR, ERCC1, ERCC2, FGF19, FGF3, FGF4, FGFR1, MDM4, MET, MYC, MYCL, NRAS and NRG1 genes were observed. The tumor was microsatellite stable, with a low tumor mutation burden (TMB) and homologous recombination proficient.
Figure 2. (a) Large, atypical cells with prominent nucleoli and associated necrosis. (b) Tumoral cells adopt an epithelioid/plasmacytoid shape, some with large, prominent nucleoli. (c-d) Intracytoplasmic vacuoles containing erythrocytes.

Figure 3. (a) Immunohistochemical staining of the tumor showing strong positivity for CD31 (immunohistochemical staining, original magnification 400x), and (b) ERG (immunohistochemical staining, original magnification 400x).
Discussion

Angiosarcoma is a rare soft tissue sarcoma that may arise from any organ, though the origin is frequently localized to the skin, liver, spleen, or heart. These lesions account for 1-2% of all soft tissue malignancies. A subset of angiosarcomas, epithelioid angiosarcoma (EAS) often presents in deep soft tissue but may arise in any location. EAS of the skin appears to affect patients from a broader age range than conventional cutaneous angiosarcoma, which typically occurs on sun-damaged skin of the head and neck in elderly patients. EASs often present with early nodal and solid organ metastases, especially to the lungs, bone, soft tissue, and skin. In the first 2 to 3 years following diagnosis, more than 50% of patients are dead of disease, but 20% to 30% of people remain disease free.

A PubMed search from 1970 to 2022 revealed 4 case reports of mediastinal angiosarcoma. Adult case series of malignant thoracic vascular tumors have also included cases of EAS. One study described 13 cases (of 52) of EAS in the thorax (lung, pleura, mediastinum, heart, and great vessels); another series described 1 case (of 16) of an EAS involving the posterior mediastinum; a final series of primary angiosarcomas of the mediastinum reported 2 cases (of 9) to have epithelioid features.

Malignant thoracic epithelioid vascular tumors are an uncommon and heterogeneous group of tumors that include low to intermediate grade EHE and high-grade EAS. The diagnosis can be challenging due to morphologic overlap, particularly on small biopsies. Variants of EAS display a range of features, from inter-anastomosing vessels lined by epithelioid endothelial cells to solid sheets of epithelioid cells where it is difficult to identify vascular morphologic features. EAS is variably positive for immunohistochemical markers of vascular differentiation, including CD31, CD34, and ERG. Immunoreactivity for cytokeratin, neuroendocrine markers and CD30 have been described and represent diagnostic pitfalls. According to Anderson et al., CD31 and ERG are the most reliable markers of vascular differentiation in these lesions, seen in 96% and 100% of cases of EHE and EAS, respectively. This case exhibited immunoreactivity for CD31, ERG and EMA.

This report is the first describing molecular findings of mediastinal EAS. A targeted massive parallel sequencing study of angiosarcomas published by Murali et al. identified MAPK pathway alterations in 18/34 (53%) of cases, involving mutations in KRAS, HRAS, NRAS, BRAF, MAPK11, and NFI, as well as amplifications in MAPK1/CRLK, CRAF or BRAF. In addition, mutations in TP53 (35%), PTPRB (29%), PLCG1 R707Q (3%), and losses of CDKN2A (26%), were also identified. Similarly, this case demonstrated NRAS and BRAF amplifications and a mutation in TP53. MYC gene amplification and overexpression has been identified in secondary angiosarcomas as well as certain sporadic angiosarcoma subtypes. These findings were replicated in this case, which also showed MYC amplification; however, to the authors’ knowledge the patient did not possess these risk factors.

The differential diagnosis of EAS in the mediastinum includes EHE, epithelioid carcinoma, epithelioid mesothelioma, and spindle cell melanoma. EHE expresses vascular markers and occasionally epithelial markers, with up to 29% of EHEs exhibiting keratin expression. Most EHE cases (90%) exhibit CAMTA1-WWTR1 gene fusions while a subset exhibits YAPI-TFE3 gene fusions. This case was CAMTA1-WWTR1 negative. Epithelioid mesothelioma is an important diagnostic consideration; an immunostain for WT1 aids this differential diagnosis.

In this case, WT1 was negative. Spindle cell melanoma may display pseudovascular spaces resembling angiosarcoma. Stains for SOX10, MelanA, and S100 were negative in this case. Finally, a mediastinal epithelioid malignancy is statistically more likely to be carcinoma than EAS, with the added pitfall of both tumors demonstrating immunoreactivity cytokeratin stains; while this case was keratin negative, the tumor cells were positive for EMA.

Suspicion of angiosarcoma and its variants in cytology/CNB cases is essential, as this is often the first sample received from a patient with a mediastinal mass. Based on published literature, CNB and incisional biopsies do not differ significantly in terms of accuracy rate. Diagnostic yields depend on the tumor’s histologic architecture. There is a significantly lower diagnostic yield for tumors with heterogeneous architecture, such as angiosarcomas and synovial sarcomas. It has been observed in some studies that incisional biopsy following non-diagnostic CNB increases the overall pathology work-up yield.

EAS may demonstrate cytologic features similar to adenocarcinoma, including tridimensional and papillary clusters, micro-acini, and singly dispersed epithelioid or plasmacytoid cells, with cyttoplasmic vacuoles, mimicking mucin. While the presence of pencillate nuclei, erythroplagocytes, and other vasoformative features are highly suggestive of vascular origin, these features are not specific, and they overlap with nonvascular neoplasms.

The prognosis of any type of angiosarcoma is relatively poor. Two and 5-year disease-free survival rates are 44% and 24%, respectively. Surgical resection with or without adjuvant radiation or chemotherapy is the main treatment modality for angiosarcoma. In unresectable cases, the median survival time is 7.3 months.
Conclusion

Although rare, EAS should be considered in patients presenting with a mediastinal mass. CNB is a reliable and effective method for soft tissue sarcoma diagnosis. Angiosarcomas tend to be more heterogeneous than other soft tissue tumors. A thorascopic or open biopsy can be considered in cases of non-diagnostic CNB in order to obtain adequate tissue for histopathology, immunohistochemistry, and molecular diagnosis.

Conflict of Interest

None of the authors identify a conflict of interest.

References

Description of Otolaryngology (OTO) Disease in Houseless Patients on O‘ahu, Hawai‘i

Enze Ma BS; Rylie M. Wada BS; Brendan K. Seto BA; Dylan S. Singh BS; Teresa L. Schiff-Elfalan MD; Lawrence Burgess MD

Abstract

This retrospective study assesses the prevalence of otolaryngology (OTO) disease in houseless patients on O‘ahu based on data from the Houseless Outreach and Medical Education (HOME) clinics, a medical student-run, primary health care service. It is important to note that this data represents only a snapshot in time of the OTO diseases present in this population. Records were examined from September 3, 2020 to September 30, 2021. Patients with at least 1 OTO disease were included in this study. A total of 597 patient records were reviewed; a total of 58 patients were included in this study. The most common OTO diagnoses in this sample were facial trauma (n = 12, 21%), dental caries (n = 7, 12%), cerumen impaction (n = 6, 10%), viral upper respiratory infection (n = 5, 9%), otitis media (n = 4, 7%), and allergic conjunctivitis (n = 3, 5%). Roughly 10% of patients seen in HOME clinics between September 2020 and September 2021 were seen for OTO disease.

Keywords

Houseless care, Otolaryngology, Student-run free clinic

Abbreviations

CAGE = Cut down, Annoyed, Guilty, Eye-opener
HNSCC = head and neck squamous cell carcinoma
HOME = Houseless Outreach and Medical Education
OTO = otolaryngology
PHQ-2/PHQ-9 = Patient Health Questionnaires screeners for major depressive disorder

Introduction

Hawai‘i has one of the highest rates of houselessness in the nation, just behind the District of Columbia and New York City, with an estimated 6458 houseless people on a given night in 2020.1,2 Multiple studies have shown that houselessness increases the likelihood of chronic diseases and other health problems.3-5 Among the houseless, there is a higher prevalence of unmet basic human needs, healthcare needs, and social needs. Taken together, these barriers often lead to a delay in or missed diagnoses, leading to worsening clinical presentations and increasing rates of mortality, morbidity, and hospitalizations.6

This study reviews data from the Hawai‘i Houseless Outreach and Medical Education (HOME) Project clinics, a primary-care medical service provided by students and faculty of the John A. Burns School of Medicine in Honolulu, Hawai‘i. The HOME Project is a mobile clinic, conducted via mobile van, that provides free medical care across the island of O‘ahu in multiple locations, 6 days a week. From September 3, 2020 to September 30, 2021, the HOME Project saw a total of 596 patients. The aim of this study is to describe otolaryngology (OTO) diseases in patients who seek care at the HOME project as it may provide some insight into the needs of patients at HOME clinic, especially as it pertains to OTO care. Although similar studies are available in other areas of the world,7-10 to date, there has been no report on the state of OTO diseases in houseless patients on O‘ahu.

Materials and Methods

The study was approved by University of Hawai‘i Institutional Review Board. Medical records of patients presenting to HOME Project Clinics between September 3, 2020 and September 30, 2021 were retrospectively reviewed and compiled into a dataset. Records with at least 1 OTO disorder in clinics across the island of O‘ahu were included in the study. OTO disorders were defined as an OTO chief complaint, ie, a chief complaint relating to ears, face (orbits, nose), oral cavity, neck, or upper airway that appeared as free text in the chief complaint section of the electronic medical record. There were no exclusion criteria in terms of age or comorbidities. Patients who returned for follow-up visit were only counted once. Diseases of the teeth and the gums were included as these conditions are often precursors for odontogenic diseases that may require evaluation and treatment by otolaryngologists. Specific diseases of the eye (ie, allergic conjunctivitis and dry eyes) were included as allergy falls within the scope of OTO.

The following information was drawn from each medical record: first and last name, age, sex, chief complaint, results of CAGE and PHQ-2/PHQ-9 questionnaires, smoking and drinking habits, and comorbid conditions. CAGE (Cut down, Annoyed, Guilty, Eye-opener) is a substance abuse screening tool, and PHQ-2/PHQ-9 are Patient Health Questionnaires designed to screen for major depressive disorder.11,12 Data were manually entered into Microsoft Excel 2022 (Microsoft Corporation, Redmond, WA).

Outcome Measures

Primary outcome measures included number and types of OTO chief complaints and OTO diagnoses. Secondary outcome measures included comorbidities, risk factors, and demographic data.

Statistical Analysis

This is a descriptive study, and no statistical analysis was utilized to interpret these data.
Results

A total of 597 patient records from September 2020 to September 2021 were reviewed. Overall, 58 patients (10%) matched the inclusion criteria and were included in the study. Characteristics of the sample are detailed in Table 1. There were 36 males (62%) and 22 females (38%) in the study. The average age was 47.9 years old (range = 18-85, SD = 13.01). Tobacco use was reported in a little over half of patients (n = 33, 57%), with 23 (40%) smoking >10 cigarettes/day. Alcohol use was cited in a total of 17 (29%) patients, with only 1 of those being female. Of the male patients, twelve (33%) reported heavy drinking, defined as >14 standard drinks/week.

The most common OTO diagnoses in this sample were facial trauma (n = 12, 21%), dental caries (n = 7, 12%), cerumen impaction (n = 6, 10%), viral upper respiratory infection (n = 5, 9%), otitis media (n = 4, 7%), and allergic conjunctivitis (n = 3, 5%). Tooth fractures secondary to trauma were counted as trauma. Tooth fractures secondary to dental disease were counted as dental caries. The full list of OTO diagnoses in the sample is detailed in Table 2.

The sample also had a wide range of comorbidities, with 53% of patients (n = 31) reporting at least 1 active comorbid condition and about 22% (n = 13) reporting 3 or more comorbid conditions. The most common comorbidities in the sample were active cardiovascular conditions and risk factors (n = 15, 26%), psychiatric conditions (n = 10, 17%), and dermatologic issues (n = 5, 9%). Six (10%) patients also reported experiencing domestic violence and 5 (9%) patients had a history of traumatic injury. Of note, some patients had more than 1 OTO disorder. Five (9%) patients reported comorbid active or previous OTO disease, including allergic rhinitis, dental issues, hearing loss, tinnitus, and tympanic membrane repair, but only the primary presenting complaint was recorded. The summative list of comorbidities in this sample is detailed in Table 3.

Table 1. Demographic Characteristics of Otolaryngology Patients Seen at the Houseless Outreach and Medical Education Clinics on O’ahu, September 3, 2020 and September 30, 2021

<table>
<thead>
<tr>
<th>Category</th>
<th>No. Patients (n=58)</th>
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<td><strong>Sex</strong></td>
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<tr>
<td>Male</td>
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<td>Female</td>
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<td><strong>Age</strong></td>
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<tr>
<td>≥70</td>
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<tr>
<td><em><em>Alcohol Abuse (CAGE</em>)</em>*</td>
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<tr>
<td>CAGE 1</td>
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<td>14%</td>
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<td><strong>Alcohol Use (Chart)</strong></td>
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<td>33%</td>
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<tr>
<td><strong>Smoking</strong></td>
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<tr>
<td>&lt;10 cigarettes/day</td>
<td>10</td>
<td>17%</td>
</tr>
<tr>
<td>&gt;10 cigarettes/day</td>
<td>23</td>
<td>40%</td>
</tr>
<tr>
<td><strong>PHQ-9</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (5-9)</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Mod (10-14)</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>Mod/Sev (15-19)</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>Severe (20-27)</td>
<td>2</td>
<td>3%</td>
</tr>
</tbody>
</table>

*a* CAGE (Cut down, Annoyed, Guilty, Eye-opener) substance abuse screening tool

*b* PHQ-2/PHQ-9 Patient Health Questionnaires designed to screen for major depressive disorder

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Table 2. Summary of Otolaryngology Disorders Identified Among Patients Seen at the Houseless Outreach and Medical Education Clinics on O’ahu, September 3, 2020 and September 30, 2021

<table>
<thead>
<tr>
<th>Otolaryngology Disorder</th>
<th>No. Patients (n=58)</th>
<th>%Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hearing loss</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Otitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Externa</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td>Media</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>Cerumen</td>
<td>6</td>
<td>10%</td>
</tr>
<tr>
<td>Vertigo</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Nose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fracture</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Oral Cavity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gingivitis</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td>Dental caries</td>
<td>7</td>
<td>12%</td>
</tr>
<tr>
<td>Herpes labialis</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td>Jaw fracture</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Palatal fracture</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Tooth fracture</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Eyes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergic conjunctivitis</td>
<td>3</td>
<td>5%</td>
</tr>
<tr>
<td>Dry eyes</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td>Orbital trauma</td>
<td>5</td>
<td>9%</td>
</tr>
<tr>
<td>Upper airway</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchitis</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td>Viral upper respiratory infection</td>
<td>5</td>
<td>9%</td>
</tr>
<tr>
<td>Neck</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical stenosis</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Goiter</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Trauma</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Folliculitis</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Forehead laceration</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td>Tinea capitis</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Post-operative pain</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>

Table 3. Summary of Comorbidities Among Otolaryngology Patients Seen at the Houseless Outreach and Medical Education Clinics on O’ahu, September 3, 2020 and September 30, 2021

<table>
<thead>
<tr>
<th>Comorbidity Type</th>
<th>No. Patients (n=58)</th>
<th>%Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disorder</td>
<td>15</td>
<td>26%</td>
</tr>
<tr>
<td>Psychiatric disorder</td>
<td>10</td>
<td>17%</td>
</tr>
<tr>
<td>Domestic abuse</td>
<td>6</td>
<td>10%</td>
</tr>
<tr>
<td>HEENT disorders</td>
<td>5</td>
<td>9%</td>
</tr>
<tr>
<td>Dermatologic disorder</td>
<td>5</td>
<td>9%</td>
</tr>
<tr>
<td>Traumatic injury</td>
<td>5</td>
<td>9%</td>
</tr>
<tr>
<td>Respiratory disorder</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>3</td>
<td>5%</td>
</tr>
<tr>
<td>Migraine</td>
<td>3</td>
<td>5%</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td>Arthritis</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td>Thyroid dysfunction</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>

Discussion

This study retrospectively analyzed data from multiple HOME clinics across the island of O’ahu. Analysis showed that roughly 10% of the population at HOME clinics were seen for otolaryngologic reasons. The most common conditions presented were trauma, followed by dental problems, cerumen impaction, viral upper respiratory infections, and otitis media, and allergic conjunctivitis. These are similar to some of the common conditions seen by primary care physicians.\(^{13}\)

Some studies have reviewed the results of OTO associated diseases within the houseless population in multiple locations. Ralli et al conducted a retrospective study in Rome which reviewed 2516 houseless patients and found that many of them suffered from OTO-related issues, the most common being pharyngotonsillitis, rhinitis, and hearing loss.\(^{7}\) Importantly, precancerous or cancerous lesions were reported in 7%. Noel et al conducted a cross-sectional study of 100 houseless patients in Toronto and found that there was a significantly higher rate of speech-frequency hearing loss in one ear (40%) and high-frequency hearing loss (52%) in the houseless population when compared to the general Canadian public (19% and 36%, respectively).\(^{8}\) Only 28% of those patients were aware that hearing tests and hearing aids were covered through social assistance programs. This may contribute to the lack of significant hearing loss patients in the data from this study (n = 1) since few may be aware that hearing tests and hearing aids are available through social assistance programs and thus may neglect to bring this to the attention of the clinic. Age may also be a factor, as the average age of the patients in this study was around 48 years old, whereas hearing loss usually has a later onset. Moore and Durden analyzed 325 houseless patients in Atlanta, Georgia...
over a 3-year period and found that 41% reported at least 1 otolaryngologic sign or symptom, with 9% having histologically confirmed head and neck cancers.9 Interestingly, while 72% of participants in this study knew that tobacco use is a risk factor for lung cancer, 79% were not aware that it is a risk factor for head and neck cancers. Wu et al examined 100 houseless adult patients in Toronto, Canada and found 22 patients with OTO needs, including 2 with head and neck cancers.10

One particularly interesting finding in this research study was the relative lack of infectious processes, such as upper respiratory infections, pharyngitis, tonsillitis, and sinusitis. In other similar studies, upper respiratory infections accounted for 22% of their patient population, whereas in this study, they accounted for only 9%.10 This may be explained by HOME’s COVID-19 pandemic protocols at the time this study was conducted. It is possible that patients with infectious processes may have been sent straight to an urgent care or alternative primary care provider, as HOME clinics were sending some patients with COVID-19 symptoms, such as fever and cough, to other facilities, in accordance with the medical school policy for minimizing risk of exposure to students. Because infectious processes may present similarly to COVID-19, some of these patients may have been missed in this data. Of note, the HOME Project has liberalized its COVID-19 protocols since then and is now able to see patients with COVID-like symptoms.

Another point to consider is the lack of potential diagnoses for head and neck malignancies, particularly head and neck squamous cell carcinoma (HNSCC). Roughly 57% of the patients in this data set were smokers, and 40% used more than 10 cigarettes (0.5 packs) per day. About 29% of the patients use alcohol, and more notably, 33% of male patients had more than 14 drinks per week. Although there was no reported instance of cancerous or precancerous lesions in the data, these patients are indeed at an increased risk for HNSCC due to increased exposure to smoking and alcohol.14 In the United States general population, the incidence of HNSCC is 11.2 per 100000 (0.012%).15 As stated previously, current literature reports a higher incidence of HNSCC in houseless populations. Ralli et al reported 7% of patients in their study population had cancerous or precancerous lesions.7

There are multiple reasons that may explain the lack of malignancies identified in the HOME Project population. Moore and Durden found 256 of 325 patients who reported at least 1 sign or symptom of head and neck malignancy, and they subsequently referred 28 of those for further OTO evaluation. The study also found that while over 70% of houseless patients knew of the connection between tobacco use and lung cancer, only 19.9% were aware that smoking is a risk factor for HNSCC.9 Given that HNSCC usually presents asymptptomatically in the early stages of the disease as small solitary lesions, patients may not discuss subtle changes in swallowing, taste, throat or ear pain, speech, and skin with the provider. It has also been speculated that medical students do not have much exposure to OTO in their clinical years, and this may contribute to a lack of recognition for HNSCC, especially if it presents early in the oral cavity or oropharynx.16 It may also be the case that HOME clinic is dominated by the acute concerns of patients and that a thorough examination of other areas is not a priority during patient encounters. Additionally, HNSCC is a diagnosis that requires biopsy and microscopic analysis, and houseless patients may have difficulty finding access to these kinds of services. Taken together, these factors may contribute to the lack of HNSCC in the data.

Although head and neck cancer screening has been largely abandoned due to lack of efficacy in the general population, targeted screening for at-risk populations, such as houseless populations, may be effective.17,18 Providing education about risk factors and early signs and symptoms may prompt individuals to seek health care earlier and prevent complications of late-stage disease.

It is also worth noting that there are considerable barriers to health care for houseless populations, particularly with insurance coverage, transportation, and other individual and environmental factors.19-21 The HOME Project seeks to address these issues by providing free, mobile care. However, without an OTO consultation, it is often difficult to formally diagnose complex diseases of the head and neck, which requires biopsy and microscopic analysis, such as for HNSCC. Therefore, it may be helpful in clinics that provide care primarily for houseless patients to have an otolaryngologist who would accept referrals for complex problems. According to one study, OTO consultation in houseless clinics were only required for 6% of all patients with OTO problems.22 The other 94% of OTO problems were addressed by primary care. Having readily available OTO consultation for the 6% of patients could prove to be crucial in diagnosing more serious disorders and providing appropriate early treatment or prevention. In this study, the most common OTO complaints were facial trauma, dental caries, cerumen impaction, viral upper respiratory infection, otitis media, and allergic conjunctivitis. Although many of these are adequately treated with primary care providers, some conditions, particularly complex facial trauma or serious cerumen impaction, may require OTO consultation. Currently, the HOME Project does not have an otolaryngologist who takes referrals for possible patients, but this may be something that may be addressed in the future.

Houseless patients are at risk for multiple medical conditions, such as heart disease, diabetes, hypertension, chronic obstructive pulmonary disease, which often require extended time for recovery and increased length of hospital stays.23 It has also been shown that patients with certain comorbid conditions, such as congestive heart disease, peripheral vascular disease, etc., have decreased chance of survival for head and neck cancers.24 This dataset of OTO patients demonstrated similar comorbidities, with hypertension and psychiatric disorders being the most
prevalent. In fact, at least 50% of the population had 1 or more comorbidities, and 22% of patients had 3 or more. The 2022 Point in Time Count for O‘ahu revealed similar comorbid conditions and risk factors, with 22% of houseless individuals reported a mental illness and 18% reported substance use problems. Furthermore, Hawaii’s finite land space and high cost of living without relative increase in compensation greatly increases financial burden, posing another barrier to healthcare access and delivery. Taken together, these data demonstrate the complexity of houseless patient care in Hawai’i and the importance of regular follow-up with these patients to avoid complications for their multiple health problems, particularly in the setting of complex OTO diseases.

Limitations

Given that these data were collected during peak COVID-19 pandemic years, the data may not capture an accurate representation of the population, as patients may have been unwilling to visit the clinic or patients may have been referred to other facilities with more resources at that time to handle possible COVID-19 exposure. Researchers were unable to extract data from previous years for 2 reasons. First, the authors are also most familiar with the clinic as it operated in the past couple years and thus, using data from recent years allowed authors to ensure data quality and completeness. Second, because of the expanding nature of HOME clinics, the electronic medical record system was changed to fit the needs of the clinic better, and data from the previous electronic medical record was unable to be obtained.

Conclusion

This study showed that roughly 10% of patients seen at HOME clinics were due to otolaryngologic conditions. It is important to note that this data serves only as a snapshot in time that describes OTO disease amongst HOME project’s patients during the COVID-19 pandemic. Given the limitations stated in the discussion, these data cannot be used to compare incidence or prevalence of OTO disease with other similar studies in the literature. The data showed that the most common OTO problems that was seen at HOME clinics were facial trauma, dental caries, cerumen impaction, viral upper respiratory infection, otitis media, and allergic conjunctivitis. An interesting further study may be to implement a screening process for head and neck cancers specifically for HOME clinics to see if any patients would be referred for further OTO evaluation. Future studies may also investigate the rate of follow-up for patients at HOME clinic for complex OTO disease.

Conflict of Interest

None of the authors identify a conflict of interest.

Acknowledgements

The authors would like to acknowledge Dr. Jill Omori, Jason Seto, and Nicholas Liu for the original data collection as well as all of the HOME staff and volunteers.

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References


A Framework that Strengthens Legislative Measures to Halt and Reverse the Pacific Non-Communicable Diseases Crisis

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Insights in Public Health is a recurring column from the public health community and is coordinated by HJH&SW Contributing Editor Mapuana Antonio DrPH from the Office of Public Health Studies in the Thompson School of Social Work & Public Health at the at the University of Hawai‘i at Mānoa and Contributing Editor Nichole J. Fukuda MS from the Hawai‘i Department of Health.

Keywords
non-communicable diseases, policy, legislation, Pacific

Abbreviations
NCDs = noncommunicable diseases
MANA = Monitoring Alliance for NCD Action
PICTs = Pacific island countries and territories
PLF = Pacific legislative framework
SPC = the Pacific Community, formerly Secretariat of the Pacific Community
WHO = World Health Organization

Introduction

It is well recognized that legislative measures are important tools of health behavioral change.1 The effective use of laws and regulations are powerful tools to address the growing burden of noncommunicable diseases (NCDs), with some of the most common being cardiovascular disease, cancer, chronic respiratory disease and diabetes.1 Many risk factors for NCDs can be minimized through multiple means, which may include restricting the availability of, or imposing taxes on products that cause harm such as tobacco, alcohol, and unhealthy foods and drinks.

At the joint Pacific Forum Economic and Health Ministers Meeting held in 2014, the ministers endorsed the Pacific NCD Roadmap, which provides specific policy, regulatory, and tax measures that can be implemented by Pacific Island Countries and Territories (PICTs) to address NCDs more effectively. The ministers also agreed to report on progress against the implementation of the roadmap at every Pacific health ministers’ meeting. To assist PICTs in monitoring progress and implementing the Pacific NCD roadmap, the Pacific Monitoring Alliance for NCD Action (Pacific MANA) was established, and the Pacific MANA Dashboard was developed. Pacific MANA is a collaborative alliance that brings together PICTs and development agencies who collect, analyze, translate, and disseminate data related to NCDs. Pacific MANA aims to provide a mechanism for coordinating and strengthening NCD monitoring across the Pacific. The Pacific MANA dashboard, on the other hand, uses a traffic light rating scheme (ie, red for no policy present, amber for policy under development, and green for policy in place) to track PICTs’ progress on policies and legislation aimed at preventing NCDs.

The Pacific MANA dashboard baseline assessment, which aimed to monitor progress on the implementation of the Pacific NCD Roadmap, was conducted for 21 PICTs between 2017 and 2018. Findings demonstrate substantial NCD-related legislation gaps that need to be strengthened in PICTs. Without urgent legislative actions, NCDs will remain the leading cause of death in PICTs due to premature mortality and disability due to NCDs. NCDs in PICTs also contribute to increased health care cost, reduced productivity and pose a major threat to health and development.6,7

It is highly likely that the burden of NCDs will continue to increase due to the socioeconomic, environmental, and commercial factors that influence the Pacific.8 For example, the food, tobacco and alcohol industries’ have penetrated markets in the region and contribute to the burden of NCDs through advertising, promotion, and sponsorship of unhealthy products that continue to undermine the efforts of combating NCDs. Alternatively, the capacity and expertise to develop and implement NCD-related laws remain limited in many PICTs. In addition, there are limited regional frameworks that guide PICTs to reform NCD related laws to address legislation gaps to cope with the changing environment and to scale up NCD actions.
**Efforts in Developing an Innovative Regional Legislative Framework**

Recognizing these challenges, the Pacific heads of health and health ministers met in 2017 and 2018 and recommended the development of the Pacific Legislative Framework (PLF) for NCDs that incorporates legislative measures of key NCD risk factors. Following the recommendations provided by Pacific health leaders, development agencies, including the Pacific Community (formerly the South Pacific Commission or Secretariat of the Pacific Community or the SPC), World Health Organization (WHO), and academic institutions, initiated the development of PLF in consultation with PICTs. An inaugural regional consultation meeting was convened in March 2019, with legal experts from 21 PICTs and health policy experts from the development agencies. During the convening, the framework was developed, including the proposed structure, approach, and contents of the PLF.

The framework specifically covers key NCD prevention and control areas including tobacco and liquor control, health promotion, promotion and protection of breastfeeding, regulation of marketing related to unhealthy food and beverages to children, reduction in the consumption of salt, sugar and trans-fat, and NCD taxation measures. In each of the areas covered, the PLF sets out 3 components: legislative policies (policy objectives for legislative provisions); a legislative plan (legal framework to guide the drafting provisions); and legislative provisions (sample guiding provisions that can assist PICTs to adapt into their own respective NCD legislations). The legislative provisions are minimum provisions that countries can adapt when reviewing NCD-related laws. PICTs can use the legislative provisions as a guide, taking into account the drafting practices and styles and the relevant laws within their jurisdictions. The framework also provides practical guidance on the process of reviewing NCD-related laws in each of the PICTs with the view to strengthening those laws. This document was presented at the Pacific health ministers’ meeting in August 2019, where it was endorsed.

The second regional consultation was held in November 2019 where legal and health policy experts from 21 PICTs, development agencies, and academic institutions identified gaps to strengthen the PLF. After a series of follow-up virtual consultations in 2020-2021, the PLF was finalized. The final PLF, a product developed through extensive and comprehensive consultations, was formally endorsed for implementation by the Pacific heads of health in September 2021 and by health ministers in March 2022. The PLF became the first ever innovative regional framework that guides PICTs to reform NCD-related laws and to harness the power of Pacific voice through collective approaches to tackle the Pacific NCD crisis.

While progress has been made with the regional framework, adaptations at a local level continue to be a challenge. There is also an urgent need for PICTs to improve their capacity for enforcing public health laws so that adaptations of the PLF at the local level are effective. Having legislation developed is 1 step, however, implementing and enforcing legislation is another step, and the latter remains a huge challenge across the region. Thus, implications at a more local level continue to be explored.

Through the endorsement of the PLF and with a series of complementary webinars facilitated by SPC and development agencies, PICTs have been upskilled to strengthen their NCD-related legislation using the PLF in developing or amending legislations in respective jurisdictions. Since the endorsement of PLF, for example, Nauru, French Polynesia, Kiribati, Solomon Islands, Tonga, and Tuvalu have identified gaps in their current liquor control, tobacco control, and other legislations with a view to strengthen them in line with the legislative provisions recommended in the PLF. More specifically, PICTs have addressed legislation gaps including regulations on alcohol advertising, marketing of unhealthy foods and sugary drinks, and tobacco industry interference. In the next few years, and after utilizing the PLF, it is expected that PICTs will have further strengthened multisectoral actions recommended in the Pacific NCD Roadmap, through updated laws and regulations, together with other behavioral change interventions for NCDs, such as awareness, education, promotion, and medical interventions.

**Conclusion**

The PLF is regionally owned and designed to guide the development of NCD-related legislation in all relevant sectors; however, engaging these sectors is still a significant challenge. Given that different government authorities deal with different NCD-related legislation, there is still a need to have an integrated government approach and commitment from the political leaders to enact evidence-based legislation. Despite some challenges, the need for PLF has become apparent as many PICTs have limited knowledge on the technical-know how of legislation development. There is a critical need to support PICTs to identify legislation gaps and utilize the framework in reforming NCD related laws to create an enabling legal environment to address key NCD risk factors. This will contribute to the halt and reversal of the Pacific NCD crisis and meet the global NCD targets particularly to reduce premature mortality from NCDs.

**Acknowledgements**

Pacific health ministers and heads of health, and legislative drafters and policy experts from PICTs, and development partners and academic institutions such as WHO, Pacific Islands Health Officers’ Associations PIHOA, Pacific Islands Forum Secretariat, McCabe Center for Law and Cancer, UNICEF, the University of Sydney, and Fiji National University, who were actively involved in the development and endorsement of the PLF are acknowledged. The authors also would like to acknowledge the Australia and New Zealand governments, and the Commonwealth Secretariat for providing financial contribution to the development of the PLF.
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References
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