A Case of Eccrine Carcinoma Presenting with Neurological Manifestations

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Abstract

Introduction: Eccrine carcinoma is an extremely rare skin tumor where only 1/13000 specimens have been submitted to dermatopathological laboratories in the United States. There is no data yet to compare the Philippines with the international incidence of eccrine carcinoma. This is a case of a 69-year-old Filipino female who presented with a recurring invasive indolent tumor at the right fronto-parietal area who presented with left sided hemiparesis and seizure.

Case: The patient was presented with a recurrent invasive indolent mass on her right front-parietal area, grossly measuring five by four centimeters, nodular flesh colored, which extended intracranially. This was associated with left sided hemiparesis and due to the extent of the tumor encroaching through the brain parenchyma, patient was noted to have seizure episodes. The patient was given surgical and radiologic options however, she did not comply and died last December 2015.

Results: A cranial MRI with MRA showed a heterogenous enhancing intracranial mass with extracranial component with compressed entrapped and depressed superior sagittal sinus by the axial mass witin calvarial penetration and scalp involvement compressing on the right parietal lobe with parenchyma edema. Biopsy was eventually done and findings were consistent with an eccrine carcinoma.

Conclusion: This is the first case of eccrine carcinoma in our institution. Due to the paucity of data, there are no guidelines to the management of an eccrine carcinoma. Hence the imperative need to raise awareness regarding this rare tumor because, without a high index of suspicion this rare entity may be overlooked or misdiagnosed. When presented with an indolent invasive recurrent tumor a high index of suspicion that an eccrine Carcinoma may be suspected. Excision biopsy may be done for correct identification of the tumor.

Keywords: eccrine carcinoma, brain parenchyma, neurological symptoms, adnexal neoplasm

Introduction

Malignant cutaneous adnexal neoplasms are a large and varied group of tumors that exhibit morphological differentiation. Some tumors are rarely aggressive and have potential for nodal involvement and distant metastasis with poor clinical outcome.[1] In particular, eccrine carcinoma which are tumors that may be derived denovo from any portion of an eccrine apparatus or a result from the transformation of an excising benign eccrine tumor. Hence, are said to be the most challenging areas of dermatopahology.[1,2] Eccrine carcinoma is a rare histologic subtype of adnexal tumors which is a rare cutaneous condition characterised by a plaque or a nodule most commonly found on the scalp, trunk or extremities.[1] These tumors grow either slowly over the years or may progress rapidly and reaching a size of several centimetres in diameter.[3] Due to the rare nature of this cancer, there is a great paucity in experience and literatures related to its treatment.[4] This paper aims to discuss a case of eccrine carcinoma presenting with neurological manifestations.

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Objectives

The objectives of this paper are as follows: 1) to discuss the history and the pertinent physical examination findings in the patient presenting with tumor in an unlikely location; 2) to discuss the pathophysiology of an eccrine tumor and the probable diferrential diagnosis, and; 3) to discuss the diagnostics and treatment regimen that may be offered to patients presenting with eccrine tumors.

Case

V.E., a 69-year-old, female, married, Filipino, Roman Catholic, born in Cavite and currently residing in Laguna. She has been admitted several times due to generalized body malaise accompanied by weakness, which then

eventually led to generalized seizure, this was primarily due to a recurring mass at the left fronto-parietal area of her head with a 11-year history.

Clinical History

Patient presented with an 11-year history of a recurrent mass initially a pea-sized located at the left fronto-parietal area of her head, it was allegedly nonmovable, non painful, well circumscribed there was no associated headache or dizziness no consult done and no medications were taken. On the same year the mass was noted to gradually enlarge which was equated to the size of a "table tennis ball" Still no consult nor were any medications taken.

Six years PTA, mass was noted to be the size of a small "golf ball" which was then noted to have ulcerations and occasional episodes of bleeding, but still non painful, non movable, no medications were taken but approximately the same year the mass was noted to have multiple ulcerations with bleeding and purulent features which prompted consult with a surgeon, Total excision and histopath was done and revealed a (5.5x 3.0 cm) malignant adnexal tumor suggesting a hidraadenoma, (A skin adnexal tumor subtype). The patient was advised chemotherapy however patient did not comply hence was lost to follow up.

Five years PTA, patient noted the recurrence of the mass allegedly at the same area (left fronto-parietal) mass was approximately the size again of a golf ball there was no associated headache, dizziness, motor weakness nor any slurring of speech, patient noted mass now not to increase in size no consult done no medications taken.

Six months PTA, patient noted a minimal enlargement of the said mass no associated headache nor dizziness was noted no consult done.

Three months PTA, mass was noted to increase in size with progression of neurologic deficits, a cranial MRI with Gadolinium revealed a probable meningioma with malignant features extracalvarial secondary to contiguous spread. During the course of admission patient was noted to have rapid progression of weakness both her lower extremities until she lost motor control over both her lower extremities this was associated with left grip weakness, and when walking she was noted to drag her left foot hence repeat Cranial MRI with MRA noted compressed entrapped and depressed superior sagittal sinus by the axial mass with calvarial penetration and scalp involvement. Medical decompression with mannitol was given but the patient noted more spasticity on the right extremities. Patient was advised to be referred to a neurosurgeon and was scheduled for a craniotomy, however, patient was noncompliant. After three days of admission, since there was no resolution in symptoms the family decided to be discharged against medical advise. Patient was maintained on decilone (Dexamethasone) 4.0 mg three times a day.

Two months PTA Patient decided to seek second opinion at the Philippine General Hospital where patient was seen by a neurosurgeon who decided to do an FNAB of the mass which revealed a cell findings consistent with a low grade malignancy. The histopathological report revealed that "An eccrine carcinoma is highly considered", patient was again advised surgery however opted to defer and was lost to follow up.

Two weeks PTA was noted to be wheelchair borne with recurrence of left sided body weakness accompanied by pain hence was given dexamethasone 5.0 mg/IV every six hours, mannitol 50ml every four hours, Repeat imaging with Cranial MRI with gadolinium, MRA of intracranial vessels and MRV was done on the third day of admission which showed heterogenous enhancing intracranial mass with extracranial component or maybe the other way around. The mass compresses on the underlying right high parietal lobe with associated parenchymal edema. The mass is also inseperable from superior sagital sinus. Patient noted persistence of pain on the left extremity hence was referred to surgery. However on preoperative evaluation patient was stratified as high risk hence relatives opted not to proceed with the surgical plan. Hence patient was advised home transfer until she was more stable for the procedure.

One day PTA patient was noted to have an increase in her sleeping pattern and with a flat affect, and was unable to feed properly, but no consult was made. No medications were taken. Few hours PTA patient was noted to have seizure episodes hence was again admitted.

Past Medical History

Patient is a known hypertensive for more than 15 years currently and is maintained on Carvedilol 6.25mg ½ tab OD, for her Ischemic heart disease she takes trimetazidine one tablet twice a day. She was also diagnosed with type II diabetes mellitus and is maintained on insulin. The patient has no other known co morbids of tuberculosis, asthma and allergies.

Family Medical History

The patient's maternal and paternal side has a history of hypertension and a history of nasopharyngeal CA in her paternal side. Other hereditary / familial diseases were not noted, such as diabetes mellitus, cancer, allergies and asthma. No one in the family has a history of any other masses.

Patient was initially admitted for 14 days managed as a case of seizure secondary to intra and extracranial mass

with concomitant pneumonia in the immunocompromised host, ischemic heart disease. Initially was drowsy GCS 10 (E1 V3 M6) but with stable vital signs (BP:120/80 HR:105 RR:20 T: 36.7˚c and an O2 saturation of 97%) Initial medications of diazepam for frank seizures, levetiracetam, mannitol 100cc via IV dexamethasone, piperacillin-tazobactam, ipratropium bromide, acetylcysteine was given for the concomitant pneumonia.

Upon physical examination, the patient had senile skin turgor and conjunctivae was pale to pink. She had a nodular mass on right fronto-parietal area of scalp soft non-movable 5x4cm well circumscribed, with hypopigmented patches on face trunk and extremities. Both lower extremities were noted to be atrophied indicative of patients' inability to ambulate. Cardiovascular findings showed an adynamic precordium normal heart rate regular rhythm. Chest and lung examination revealed symmetrical chest expansion with intercostals retractions with decreased breath sounds on the left lower lung field and fine crackles on both lung fields and no wheezes were noted. Patients abdomen was soft normoactive and nontender. Findings in the extremities noted no limitation in range of motion patient had atrophy of both lower extremities but pulses were full and equal. Patient was drowsy but conversant however, with incomprehensible speech. Cranial nerve examination showed no anosmia, pupillary reflex was 2.00 mm EBRTL pupils, with intact direct and consensual pupillary reflex on both eyes. Fundoscopy was done and a clear media with an artreriovenous ratio was noted,[2;3] flat disc distinct disc boarders, no haemorrhages and intact EOMs movements. Symmetrical facial movement decreased, gross hearing, able to swallow, intact but weak gag reflex, uvula was in midline patient, weak left shoulder shrug and patient's tongue is midline on protrusion with no fasciculations, nor atrophy noted. Upon examination of the Motor System patient had intact muscle tone on left upper and lower extremities, Upon gross motor examination patient was noted to have 2/5 on left upper extremities 0/5 on left lower extremities 5/5 on right upper extremities 5/5 on right lower extremities . The left upper and lower extremities were Spastic. Patient has no sensory deficits to pain, temperature, position sense and vibration on all extremities. Patient was hyperreflexive on the left extremities and normoreflexive in right extremities. No neck rigidity was noted hence, patient was initially placed on O2 inhalation via nasal cannula. Nasogastric tube (NGT) was inserted, Initially treated as seizure disorder secondary to malignant brain tumor and pneumonia in the immunocompromised host.

Patient was also referred to an oncologist due to the cranial mass. He then recommended either surgery or radiation therapy. Option 1. Surgery involved significant risk but without assurance of total resectability 2. Radiation therapy was less invasive however no current therapeutic claims may be benefited out of radiation for a mucinous type of carcinoma. Patient was referred to radio oncologist when seen the plan was for the patient to undergo CT based RT planning initially, followed series of radiation, patient and her relatives were adamant regarding the procedure and opted surgical options. However due to the intraparencymal invasion of the tumor surgical options were unfavourable at the time. Since some studies[5,6] have not showed benefits in chemotherapy and radiotherapy of eccrine tumors these options were not advised.

The patients crainial MRI (Figure 1) showed heterogenous enhancing intracranial mass with extracranial component. The mass compresses on the underlying right high parietal lobe with associated parenchymal edema. Mass is also inseparable from superior saggital sinus.

Repeat cranial MRI with MRA noted compressed entrapped and depressed superior sagittal sinus by the axial mass with calvarial penetration and scalp involvement.

FNAB of the mass was done and revealed a low grade malignancy, eccrine carcinoma is highly considered.

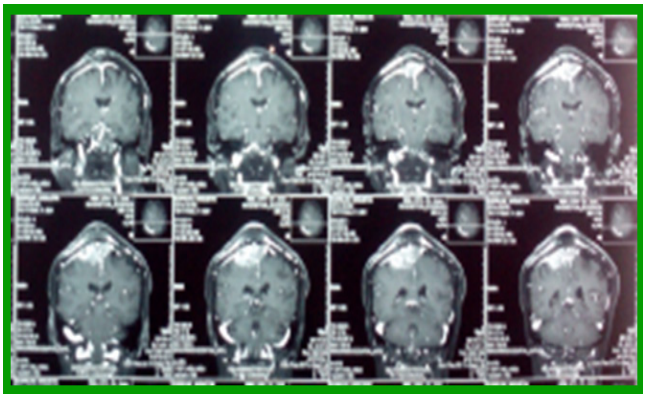

Figure 1. Patient's MRI showing heterogenous intracranial mass

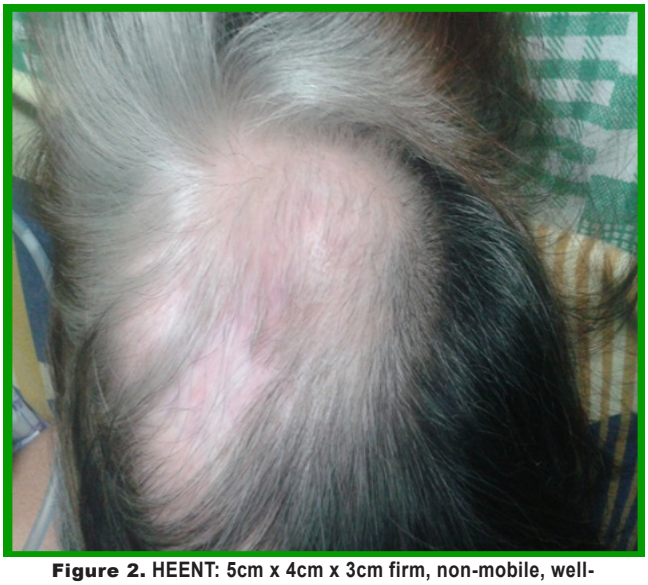

Figure 2. HEENT: 5cm x 4cm x 3cm firm, non-mobile, well-circumscribed mass at right parietal area

Electroencephalogram Findings:

1. Diffuse delta theta slowing of background activity consistent with an encephalopathic process
2. Area of focal slowing over the right vertex and temporal areas
3. Intermittent theta sharp potentials over the right temporal area.

Discussion

Skin adnexal carcinomas are a spectrum of benign and malignant tumors that exhibit morphological differentiation towards different type of adnexal epithelium present in normal skin either the pilosebaceous unit, eccrine or apocrine. However what makes skin adnexal complicated is the fact that they may exhibit more than one type of differentiation.[7]

Normal histology of skin appendages is that it comes from the ectoderm at fourth week of development a single thick ectoderm and underlying mesoderm begin to proliferate and differ towards various structures including skin adnexal structures, thus, these specialized structure located within the dermis including the deep dermis and locally within the subcutaneous fatty tussue represented by three histologically distinct structures the pilosebaceous unit, eccrine sweat glands and apocrine glands vary to form one part of the skin to another. The distribution and arrangement of these appendages vary from one part of the skin to another, but the overall general basic morphogenesis is maintained.

The initial differential diagnosis was a *Chondroid syringoma,* which is a mixed tumor of the skin uncommon adnexal neoplasm abd behaves in a benign manner where the most common location is the head and neck regions, but malignant counterpart notes to be more common in the trunk and extremities. Diagnosis is based upon histopathological characteristics, this type of tumor which has a propensity for malignant differentiation but metastatic spread may be via hematogenous or lymphatic routes. In our observation, this was not consistent with what we saw in this patient and histological findings were strong factors to rule out this type of tumor.

The second differential is pilomatrical carcinoma which is another adnexal tumor, a rare tumor with a predilection for the head and neck. Its age of incidence is bimodal, but is noted to be more common in the first two decades of life, prevalent among males. Other characteristics of this tumor is that they generally appear as solitary tumors however multiple or recurring tumors have been reported in association with myotonic dystrophy.[8] Another differential diagnosis was hidraadenoma which presents as a well circumscribed tumor, consisting of one or more tumorous nodes, which may present as a solid, cystic, tubular mass.[1] Upon microscopy Solid areas contain several kinds of cells: pale (or sometimes clear) cells and dark (with eosinophilic cytoplasm), sometimes squamoid and mucinous cells are present as well.[9] Cystic areas usually contain eosinophilic amorphous material. The lining is flat. Tubules are lined by cubic or cylindric epithelium. Mitotic activity is present even in benign tumors, the diagnostic criteria of malignity are cellular polymorphism and invasive growth. Which on biopsy was not evident in the patient discussed in this case report. But its malignant counterpart however, the a Malignant hidradenoma, which is a rare neoplasm which is slow-growing, painless papule or nodule on the head, neck, or extremities incidence between 50 and 70 years of age. The tumor may grow slowly for a long time but suddenly increase in size, thus prompting the patient to seek treatment lesions may be red and ulcerated, this tumor has the propensity to invade locally.[3] However this patient showed no ulceration nor any lesions and a biopsy done showed tissue consistent with an eccrine carcinoma.[10]

The clinical scenario presents a 69-year old female who came in with a chief complaint of left-sided body weakness. She initially presented with an asymptomatic tumor on her scalp for approximately 11 years with no associated fever, but which was then accompanied by progressive left wrist pain associated with generalized body malaise and left sided body weakness. The tumor measured 5x4cm in widest diameter, non-movable with a smooth contour, well circumscribed and with no ulcerations nor erythema was noted. This tumor was noted to extend intracranially which then resulted to left-sided body weakness and seizure.

Eccrine carcinoma is a rare cutaneous lesion characterized a plaque like nodule located on the scalp trunk or extremities which are slow growing.[11] Eccrine type of carcinoma come from the genre of epithelial cyst which are common lesions formed by the down growth and cystic expansion of the epidermis of the epithelium forming the hair follicle. These cysts are filled with keratin and variable amounts of admixed lipids lipid containing debris derived from sebaceous secretions. The eccrine unit is a type of differentiation of skin adnexal tumors, which are a part of the the adnexal epithelium present in normal skin. The other two types of differentiation in skin adnexal epithelium which comes from the pilosebaceous unit and apocrine unit. Clinically, they are subcutaneous well-circumscribed firm and often movable nodules when large they may be dome shaped and flesh colored and become painful upon traumatic rupture Histologically epithelial cysts are divided into several types according to the structural components of their walls.[1] When symptomatic, common findings include numbness, tenderness, anesthesia, paresthesia of the affected site which can relate to the frequent perineural invasion of the tumor.[9] This description is consistent of that of what we observed in this case discussion. A patient with a

well circumscribed recurrent nodule dome shaped and flesh colored tumor located at the left frontro parietal area of her head, When biopsy of the tumor was done histopathological findings showed clusters and sheets and dispersed round to ovoid cells with prominent nucleoli with a consistent with the cytopathological diagnosis of eccrine carcinoma. The adnexal neoplasm has a wall nearly identical to the epidermis and is filled with laminated strands of keratin the pilar to tricilemmal cyst has a wall that resembles follicular epithelium. The dermoid cyst is a similar to epidermal inclusion cyst but it also shows multiple appendages budding outward from its wall. Finally stetocystoma multiplex constitutes a curious cyst with wall resembling the sebaceous cyst.[1]

There are literally hundreds of benign neoplasms arising from adnexal structure. Although some show no aggressive behavior and and remain localized they may be confused with certain types of cutaneous cancers Certain adnexal tumors are associated with Mendelian patterns of inheritance and occur as multiple disfiguring lesions.[12] Eccrine and aporcine are often confused with metastatic adenocarcinoma to the skin because of their tendency for abortive gland formation.[1] However, it is important that eccrine carcinoma should be considered as a differential diagnosis in patients older than fifty years old with long standing tumors in the limbs and head.[13] Other subtypes of eccrine carcinoma exists such as mucinous eccrine carcinoma, eccrine porocarcinoma and MAC.[14] Basically, microscopy may be imperative in diagnosis however alone it is insufficient to establish an eccrine lineage neoplasm because there is no specific miscroscopic features.[13] Eccrine gland carcinomas posses no distinctive clinical features making diagnosis by gross appearance virtually impossible. They usually manifest as non-tender, subcutaneous nodules, primarily in elderly individuals as earlier mentioned. Individual malignant cells are rich in glycogen and stain with PAS and are diastase sensitive with prevalent nuclear changes and propensity for lymphatic invasion.[15] Studies have suggested the use of immunohistochemistry (p53) however it does not distinguish cutaneous eccrine tumors form cutaneous metastases hence clinical and radiologic correlation is critical.[5]

MAC (Microcystic Adnexal Carcinoma) is a locally aggressive neoplasm, which is a subtype of an eccrine carcinoma which occurs in middle aged to elderly patients. Which, if we were to subclassify the type of eccrine carcinoma it would be a good differential. It was first described in 1882 by Goldstein et al. It is also synonymous to malignant syringingoma, even an eccrine adnexal tumor. MAC is generally slow growing a solitary nodule flesh colored plaque or nodule with indistinct boarders Lesions may be assymptomatic but if symptoms do occur they may include numbness burning anesthesia or perinuclear invasion.[9] It is also said to be an aggressive locally destructive cutaneous appendageal neoplasm with high rate of local recurrence.[9] It occurs Predominantly in the white population with predilections for the head and neck,[15] But unlike the other primary cutaneous malignancies MAC has a slight female predominance.[9] MAC is locally aggressive The rule in criteria would be the solitary nodule which occurs in middle aged to elderly patients with a predilection for the head and neck consistent to this patient. MAC has a clear prediection for the head and neck (86-88%) particularly the central face (73%). Histologically MAC is a tumor of pilar and eccrine differentiation.[9] Hence in recent literature it has also been synonymous with that of an eccrine carcinoma.[10,16] The histological findings for MAC is nest and cords of small bassaloid cells and scant keratin, the histological findings of the patient discussed in this case showed clusters, sheets and dispersed round to ovoid cells with prominent nucleoli similar to an eccrine carcinoma/ MAC.[11]

The invasion of the tumor into the brain parenchyma which was evident in the MRI showing that, the mass compresses on the underlying right high parietal lobe with associated parenchymal edema. The evident parenchymal edema may explain or is the most likely reason for the patients seizure, which may have resulted from abnormal neuronal discharge. Lesions of the Parietal lobe may lead to a variety of clinical phenomena such as a Corticosensory syndrome and sensory extinction, Mild hemiparesis which may be variable Homonymous hemianopsia or visual inattention, Abolition of optokinetic nystagmus with target moving toward the side of the lesion, Visuospatial disorders topographic memory loss and confusion to name a few.[15] In this case the patient she noted progressive left sided body weakness which eventually led to difficulty in ambulation, Although no other parietal lobe deficit were noted in this patient such as the homonymous hemianopsia MRI findings proved that the neoplasm extended to the parietal lobe where on repeat Cranial MRI with MRA noted compressed entrapped and depressed superior sagittal sinus by the axial mass with calvarial penetration and scalp involvement.

Treatment of eccrine carcinomas is difficult, not only due to the paucity of data, but recent randomized controlled trials are lacking to guide proper therapy. Management currently involves excision with Mohs micrographic surgery when feasible.[9]

Results

Given the rarity of eccrine carcinoma and the variable prognosis reported in the literature there has still yet to be an apt protocol for management. However current data suggests that surgery is the first choice for management of such eccrine carcinoma but since this type of cancer typically recurs there is a fair response to chemotherapy and radiotherapy.[16] There also have been current data that states that wide deep surgical excision of the tumor with fine margins should offer a reasonable chance of a long term

control of an eccrine Carcinoma.[17] Treatment modalities used for MAC include Wide local Excision, Mohs micrographic surgery, RT and chemotherapy, Current standard of care is to surgically remove the tumor in its entirety whenever feasible. This task can be challenging in clinical practice because the tumor often extends microscopically centimeters beyond the clinical apparent margins.[9] Margins reported in the literature for WLE vary from a few millimetres to 3.0-5.0 cm. Extirpation of tumor by MMS (Mohs micrographic surgery) may prove beneficial for the management of eccrine Carcinoma.[9] However there is still a high recurrence rate.[8] Recurrence rates vary significantly between the two surgical techniques with rates after WLE and MMS ranging from 40% to 60% and 0% to 12% respectively.[8] RT has been used as mono or adjuvant therapy for eccrine carcinoma however in case reports results weren't favourable.[8,16,17] Bier- Laning et al. Reported an unsuccessful trial of chemotherapy (Cisplatin and 5FU) in the management of MAC, (a subtype of eccrine carcinoma).[8] During an annual convention done in 2012 (Avraham et al.) discussed a report which studied the risk factors and survival of patients with eccrine using a large population-based database, to provide useful information for the optimal management of this disease. The researchers used data from the Surveillance, Epidemiology, and Ends Results (SEER) 17-registry database, which houses relevant data from about one quarter of the population in the United States. The cohort consisted of 1,045 patients diagnosed with eccrine carcinoma from 1973 to 2008. Carcinoma subtypes were microcystic adnexal carcinoma (32%), general eccrine adenocarcinoma (23%), hidradenocarcinoma (22%), porocarcinoma (19%), and spiradenocarcinoma (4.0%). The researchers analyzed patient demographics, histologic subtype, use of adjuvant radiation, and the stage, size, and location of tumors. Overall survival at a median follow-up of 48 months was 78%. Age-adjusted survival, according to 2000 census data, was 94%. In 92% of cases, patients were treated with surgical resection, either alone (85%) or in combination with radiation (7.0%). Five-year overall survival rates were similar (78.0% and 75.7%, respectively), and were not statistically significant. Although node-staging data were available for only 10% of patients, node positivity was significantly associated with decreased survival (P = .02). Well- or moderately differentiated tumors were associated with better five-year overall survival, compared with high-grade disease (P = .005). No associations were found between overall survival and ethnicity, tumor size, or tumor location. Adjuvant radiotherapy has not been found to be effective in controlling recurrent or metastatic disease. The benefit of regional lymph node dissection is uncertain.[18] Hence to date management with regards to eccrine Carcinoma is still conflicting.[3,16,18,19]

Conclusion

Cutaneous mucinous eccrine carcinoma is a tumor characterized by histocytologic features and abundant extracellular pools of mucin. Without a high index of suspicion, this rare entity may be overlooked or misdiagnosed. Numerous benign and malignant mucin-producing primary and secondary tumors exist and immunohistochemistry stains offer limited benefits in differentiating them. Cytologic diagnosis of primary mucinous carcinoma of the skin is possible; however, it would be best if there is correlation of clinical, radiologic and pathologic features which is necessary to arrive at an accurate diagnosis. The correct identification of the origin of the tumor is of utmost importance for appropriate therapy and prognosis. In this patient given the histopathological findings and cranial MRI and the behaviour of the tumor, we were convinced that it was an Eccrine Carcinoma, Supposedly a Wide local excision was deemed curative however it was not amenable for the patient due to the extent of the tumor, and unstable comorbid conditions (IHD, CAD and DM) there is still yet data to be published to confirm the use of Radiotherapy and Chemotherapy. Hence the imperative need to raise awareness that this tumor exists. Patient succumbed to the disease December 2015.

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