Microcystic adnexal carcinoma (MAC) is an infiltrative rare cutaneous neoplasm for which there are no consensus management guidelines because of the paucity of evidence-based practice; hence, the utility of their management is based only on previously published case reports (Waqas et al., 2017; Tanese et al., 2019). MAC usually presents as a firm dermal papulonodule or flesh-colored plaque on the head or neck. The deeply penetrative growth pattern, coupled with the long latency of MAC, poses a significant diagnostic challenge to histopathologists and surgeons. Tissue invasion may extend beyond the visible clinical margins of the mass seen on the skin surface and may also invade the underlying subcutis or even deeper into soft tissue hence, local recurrence is common. A recent systematic review recommended a deep biopsy specimen that includes subcutaneous fat to help achieve an accurate diagnosis (Worley et al., 2019). Risk factors for MAC are unknown, however ultraviolet light, radiation, immunosuppression, and genetic predisposition have been implicated in the pathogenesis (Abbate et al., 2003; Worley et al., 2019). The most commonly utilized treatment modalities include wide-local excision, Mohs micrographic surgery, and radiation therapy (RT) (Chaudhari et al., 2015).

2. Case presentation

A 41-year-old male Filipino nurse, who had no known medical history and was a smoker, presented with a localized 5-cm mass at the vertex of his scalp that had appeared 6 months ago. It was gradually increasing in size. The swelling was first observed after head trauma when the swelling transformed into a vascularized hematoma. The patient had a history of multiple head injuries and keloid formation at 10 years of age. On examination, the lesion showed grayish discoloration, with an irregular surface, obscuring borders, and scattered nodularity over 7 × 8 cm at the vertex. There was associated localized alopecia, ulceration, and necrosis (Fig. 1A). Upon investigation, the patient was found to have multiple episodes of high blood pressure, reaching 182/106 mmHg, with a positive family history of hypertension and paternal lung cancer.

In July 2018, the patient was referred to a plastic surgeon for evaluation of the scalp lesion and further management (Fig. 1A). Complete physical examination including a relevant neurologic assessment, regional lymph node assessment, and baseline imag-
ing was performed to assess for local or nodal metastasis and assist in preoperative planning. Computed tomography (CT) brain showed a right-sided, well-defined, ovoid, heterogeneous, subcutaneous lesion measuring $3 \times 2.5 \times 2$ cm in the high parietal region. Its average density was approximately 60 HU. The underlying bone appeared intact with no evidence of cortical thickening or erosion. Consequently, the patient was admitted for incisional biopsy, revealing a microcystic adnexal carcinoma with perineural invasion. Tumor cells were positive for CK7 and CK5/6, but negative for CK20 and SMA. The case was discussed with the tumor board, who recommended surgery as the initial management.

In December 2018, CT brain showed interval worsening of the right parietal extracranial soft tissue scalp lesion, with an increase in size ($2.3 \times 4.5 \times 4.8$ cm [craniocaudal (CC) × anteroposterior (AP) × transverse (TR)], involving subcutaneous tissue and overlying skin. CT chest abdomen pelvis (CAP) and mammograms showed no evidence of metastasis.

On follow-up in February 2019, CT brain showed an interval increase in size of the previously seen subcutaneous, right parietal lesion. The lesion measured $3.6 \times 6.1 \times 5.1$ cm (CC × AP × TR) with no frank involvement of the underlying bone, and no erosions or sclerosis depressed the lesion. The lesion showed heterogeneous enhancement on post-contrast study. No intracranial extension or brain metastases were noted. A wide local excision was performed with 2-cm safety margins. Intraoperative frozen sections were taken and resulted negative margin except for occipital periosteum and as a result, a neurosurgeon joined surgery for outer and inner table skull drilling exposing the dura in the center of the defect. The specimen was then sent for histopathology examination. Defect reconstruction with a split-thickness skin graft was performed temporary during the same operative session and to be booked for second stage reconstruction. Postoperative pathological examination confirmed that the surgical margins of the excised tumor were tumor-free except for occipital periosteum. The pathological report revealed microcystic adnexal carcinoma with undifferentiated foci, with a maximum tumor dimension of 6.5 cm, perineural invasion, and no lymphovascular invasion was detected. Three weeks later, the patient was admitted for skin graft necrosis in which the debridement was performed intraoperatively.

In June 2019, the scalp tumor recurred in multiple areas around the surgical scar with bilateral cervical lymphadenopathy, where the largest is located at the left level V measuring 1.6 cm on CT scan. The case was discussed with the tumor board once again. Administration of three cycles of chemotherapy, docetaxel + cisplatin regimen followed by radiation therapy (RT) was recommended. Following chemotherapy, a good response was noted in the scalp lesion along with the cervical lymph nodes based on the CT scan results. However, the patient lost follow-up due to the extensive disease recurrence resulting to delayed RT as the patient returned to his home country for 2 months. Nevertheless, the local control of chemotherapy was preserved and an updated CT scan showed no evidence of gross disease. The patient started on RT course of 66 Gy in 33 fractions using intensity-modulated RT to the primary site along with cervical lymph nodes (Fig. 3). Clinical response of the tumor was observed as early as 6 weeks after completion of RT. Follow-up scans demonstrated a decrease in the size of the previously visualized nodes, with no cervical lymphadenopathy (Fig. 2B). The patient remains asymptomatic and disease free after 18 months of follow-up. Even at the time of writing this manuscript, this was evident on the clinical and radiological imaging that was taken Fig. 4.

3. Discussion

Microcystic adnexal carcinoma (MAC) is an uncommon tumor and was first described by Goldstein and colleagues in 1982 (Goldstein et al., 1982). Predominantly, MAC occurs in a population with fair skin and usually in the head and neck region (Chiller et al., 2000; Abbate et al., 2003; Stam et al., 2015; Oyasiji et al., 2018). Due to the rarity, limited exposure, frequent extensive subclinical involvement and slow growing nature of MAC, prognosis and management strategies are not well established. Given these diagnostic challenges, the clinical presentation of MAC can be mistaken for basal cell carcinoma, squamous cell carcinoma, or other variable diagnosis reported in the literature. Hence, skin cancer screening should focus on high-risk anatomical areas, such as the scalp, where detection can be delayed because of hair covering.

This study reported a 41-year-old male patient, a finding concordant with that of Oyasiji and colleagues in 2018 and Blake and colleagues in 2010 (Blake et al., 2010; Oyasiji et al., 2018). However, this result was in contrast with other studies such as Worley and colleagues (2019) and Barnes and Garcia (2008) (Barnes and Garcia, 2008; Worley et al., 2019). In a recent systematic review conducted on gender distribution, a female predominance was shown with a median age of 61.8 years for the
The etiology of MAC is unknown nevertheless, possible triggers such as ultraviolet light and radiation have been postulated to their development (Abbate et al., 2003; Worley et al., 2019). Nonetheless, our patient had no exposure to radiation or a history of long hours of sunlight exposure. Because of the widespread infiltration and indistinct depth of invasion of the disease, it may also extend into deeper underlying structures such as muscles, nerves, and bones, leading to deformity (Abbate et al., 2003; Waqas et al., 2017). In 2000, Chiller and colleagues demonstrated that the actual tumor defect can have four-fold increase in size (Chiller et al., 2000). In our case, a clearance margin of 2-cm of the clinically apparent borders of the tumor was observed.

The mainstay treatment modality for MAC is wide local excision along with comprehensive marginal excision while preserving function and cosmesis (Waqas et al., 2017; Worley et al., 2019). As a consequence, this patient underwent complete excision with 2-cm clear surgical margins. Since the tumor was deeply infiltrative, neurosurgery was involved even though no evidence of infiltration to the skull was detected on the imaging. Tissue processing by frozen section to ensure negative peripheral and deep margins and as well as final histopathology were also performed. Nevertheless, the occipital periosteum remained positive owing to the deep infiltrating growth pattern of the tumor. Given the significant soft-tissue defects after tumor resection, reconstruction was performed using a skin graft.

Due to scarcity and diversity of cases treated with radiation therapy (RT) establishing the exact role of RT in MAC would be challenging to interpret. Our experience builds on previously published data reporting its efficacy, summarized in Table 1. The role of adjuvant RT has not been well defined in MAC. However, a number of case series have supported its use in the context of high risk factors such as close or positive surgical margins, persistent occult tumors at the margins, and perineural invasion. RT may also be beneficial in the definitive setting as a surgical alternative (demonstrated in Table 1). In this case, we administered a dose of 66 Gy in 33 fractions to 2.5 cm beyond the primary tumor location, the borders of surgical bed, cervical lymph nodes bilaterally, and the node at risk to maximize the locoregional control and had no serious adverse events documented. This is in accordance with a recently published systematic review that recommended the use of adjuvant RT (60–66 Gy, 2 Gy per fraction) in the presence of adverse pathologic features (Worley et al., 2019).

In comparison with other case reports, 45 Gy was administered by Waqas and colleagues (2017), 50–60 Gy by (Wang et al., 2017) with 100 % locoregional control, and 55 Gy given by Baxi and colleagues (2010) with 93% locoregional control, despite 69% and 56% having positive margins and perineural invasion, respectively. In other published case reports on MAC using upfront definitive RT as a surgical alternative such as those of Gulmen and Pullon (1976), (Schipper et al., 1995), Stein and colleagues (2003), Pugh and colleagues (2012) and Kim and colleagues (2012) only those of Stein and colleagues (2003) and Pugh and colleagues (2012) described positive clinical outcomes. In the recent report of Kim and colleagues (2020), a patient with 12-year history of a histologically diagnosed MAC philtrum nodule presented with worsening numbness of the upper lip and midfacial induration, was treated using RT (70 Gy) targeted to the primary site as well as the nodal area and with concurrent chemotherapy, a progression-free for 6 years from the completion of the treatment was observed (Kim et al., 2019). Moreover, in 2014 Kim and colleagues reported the use of adjuvant RT and demonstrated efficacy in treating scalp lesions (Kim et al., 2014).
In addition to RT, we incorporated sequential chemotherapy as it could potentially act as a radiosensitizer to improve local control of the treatment. Although the time period between the last chemotherapy dose and the start of radiation was 2 months, local control of chemotherapy was still preserved, clinically and radiologically. Nonetheless, as summarized in Table 2, the role of

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**Fig. 3.** Radiation plan for treatment of microcystic adnexal carcinoma primary tumor and cervical lymph nodes in (A) coronal, (B), axial and (C) sagittal view.

**Fig. 4.** Timeline of the case.
| Author (date)          | Age/Sex | Primary tumor site                          | Primary treatment                                      | TTR (month) | Nature of recurrence | Salvage treatment                                                                 | Outcome                          |
|-----------------------|---------|---------------------------------------------|--------------------------------------------------------|-------------|----------------------|-----------------------------------------------------------------------------------|----------------------------------|
| **Definitive Radiotherapy** |         |                                            |                                                        |             |                      |                                                                                   |                                  |
| Kim et al. (2020)     | 73/M    | Philtrum                                   | RT to primary (70 Gy) + lymph node (56–63 Gy) + chemo; declined surgery | NA          | NA                   | NA                                                                                | No tumor progression at 72 mo    |
| Pugh et al. (2012)    | 53/F    | Upper lip                                  | RT (63.6 Gy)                                           | 48          | Primary site         | RT (64 Gy) Total rhinectomy, partial septectomy/turbinectomy                      | Disease free at 15 mo            |
| Stein et al. (2003)   | 76/F    | Right nasal dorsum                         | RT (58 Gy)                                             | 6           | Primary site extend  | to right medial cheek + left nasal dorsum                                         | Disease free at 14 mo            |
| Schipper et al. (1995)| 65/M    | Tongue                                     | RT (NR): refused surgery RT to primary (60 Gy) + lymph node (50 Gy) | NA          | NA                   | NA                                                                                | No change in tumor size. Disease free at 21 mo |
| Gulmen and Pullon (1976)| 35/F  | Left lower lip + submental lymph node       |                                                        |             |                      |                                                                                   | Disease free at 6 mo             |
| **Adjuvant Radiotherapy** |         |                                            |                                                        |             |                      |                                                                                   |                                  |
| Brent et al. (2018)   | NS      | Orbit                                      | complete orbital exenteration with positive margin + RT (66 Gy) | NA          | NA                   | NA                                                                                | Mass reduced in size with remnant post-RT scarring. Disease free at 12 years    |
| Waqas et al. (2017)   | 59/F    | Scalp                                      | Surgical excision with positive margins + RT (45 Gy)   | NA          | NA                   | NA                                                                                | Disease free at 3 years          |
| Waqas et al. (2017)   | 53/M    | Left temporal scalp                        | Surgical excision with positive margins + RT (45 Gy)   | NA          | NA                   | NA                                                                                | Disease free at 3 years          |
| Chaudhari et al. (2015)| 14/M  | Right medial upper lip + submandibular lymph node | Surgical excision + sentinel lymph node biopsy + RT + chemo (NR) | NA          | NA                   | NA                                                                                | Disease free at 3 years          |
| Kim et al. (2014)     | 56/F    | Scalp                                      | Surgical excision with positive margins, PNI, and peristeal involvement > Wider excision + RT (NR) | NA          | NA                   | NA                                                                                | Disease free at 3 years          |
| Pugh et al. (2012)    | 60/F    | Chin                                       | MMS with NR muscle and PNI > surgical excision with reconstruction of lower lip + RT (66 Gy) | NA          | NA                   | NA                                                                                | Disease free at 30 mo            |
| Pugh et al. (2012)    | 63/F    | Right cheek                                | Surgical excision with positive margin and PNI + RT (60 Gy) | NA          | NA                   | NA                                                                                | Disease free at 26 mo            |
| Baxi et al. (2010)    | 14 patients, median age 71 years           | Head and neck region                                 | Surgical excision (56% PNI, 69% positive margins) + RT (median dose 55 Gy) | Median follow up of 5.4 y. Crude local control rate of 93%. One pt with local recurrence (CN V salvaged > RT (35 Gy) > progressed after 2 years > surgical excision + RT(45 Gy). One pt with ipsilateral cervical nodal recurrence 18 months after RT > nodal dissection > RT (60 Gy). Both diseased free | NA          | NA                   | NA                                                                                | Disease free at 26 mo            |
| Ong et al. (2004)     | 89/F    | Right eyebrow                              | Surgical excision with positive margin (declined further excision) + RT | NA          | NA                   | NA                                                                                | Disease free at 6 mo             |
| Kirkland et al. (1997)| 55/F    | Nasal septum                               | Surgical excision with positive margins + RT (55 Gy)   | NA          | NA                   | NA                                                                                | Disease free at 6 mo             |
| Yuh et al. (1991)     | 51/M    | Left lower lip                             | Surgical excision with positive margins + RT (57.5 Gy) | 36          | Primary site with    | Surgical excision + RT                                                           | Disease free at 18 mo            |
|                       |         |                                            |                                                        |             | invasion of mandible |                                                                                   |                                  |
|                       |         |                                            |                                                        |             |                      |                                                                                   |                                  |

(continued on next page)
| Author (date)            | Age/Sex | Primary tumor site | Primary treatment                                           | TTR (month) | Nature of recurrence                  | Salvage treatment                                           | Outcome                                      |
|-------------------------|---------|--------------------|-------------------------------------------------------------|-------------|---------------------------------------|-------------------------------------------------------------|---------------------------------------------|
| Birkby et al. (1989)    | 51/M    | Left lower lip     | Surgical excision with positive margins + RT (57.5 Gy)     | 36          | Primary site + ipsilateral mandible invasion | MMS + partial hemimandibulectomy + RT (61.2 Gy)           | Disease free at 18 mo                      |
| Haga et al. (2019)      | 78/F    | Philtrum           | Surgical excision                                           | Unknown     | Unknown                               | RT (60 Gy)                                                  | Recurrence at primary site and ala of the nose. Chemo (5-1 monotherapy) at 6 years for recurrence. NP at 15 mo. |
| King et al. (2018)      | 3 NR    | Surgical excision  | Unknown Primary site                                        | NR          | NR                                    | Surgical excision + RT                                      | 2 had progressive disease with 1 developing fatal metastases to skin, lymph node, and lung. Surgical excision + RT (58 Gy). Disease free at 18 mo |
| Mamic et al. (2018)     | NR      | Surgical excision  | 36 Primary site                                             | Primary site | Surgical excision with positive margin | Superior orbitotomy + RT (61.2 Gy)                         | Local recurrence 24 mo after RT > Exenteration. Developed mesencephalon and cavernous sinus metastases 21 mo later. Managed with supportive care. Recurrence at 4 mo > surgical excisions + RT (57.6 Gy). Third recurrence over left cheek treated with RT (45 Gy). Disease free at 71 mo. |
| Gomez- Maestra (2009)   | 75/F    | Right eyebrow      | MMS                                                         | 24          | Right supraorbital nerve               | Superior orbitotomy + RT (61.2 Gy)                         | Local recurrence 24 mo after RT > Exenteration. Developed mesencephalon and cavernous sinus metastases 21 mo later. Managed with supportive care. Recurrence at 4 mo > surgical excisions + RT (57.6 Gy). Third recurrence over left cheek treated with RT (45 Gy). Disease free at 71 mo. |
| Clement et al. (2005)   | NR      | Surgical excision  | 8 Primary site + positive margin and PNI                    | 8           | Primary site                          | MMS                                                         | Disease free at 71 mo.                      |
| Clement et al. (2005)   | NR      | Right canthus      | Surgical excision                                           | 7           | Right lateral upper eyelid            | Multiple surgical excisions with positive margin + RT (60 Gy) | Disease free at 47 mo.                      |
| Sebastien et al. (1993) | NR      | Chin               | MMS                                                         | 60          | Primary site                          | MMS                                                         | MMS + adjuvant RT (55 Gy) for local recurrence 48 mo later. Disease free at 16 mo. |
| Carroll et al. (2000)   | NR      | Left upper forehead | MMS                                                         | 5           | Satellite deposits (3 new distant nodules in scalp from primary) | MMS                                                         | 3 months later developed 5 satellite deposits on scalp > RT (60 Gy, 6 megavolt scalp) > developed left postauricular nodal recurrence 3 mo later. Underwent MMS but found to have lymph node infiltration. Expired shortly after from metastatic small cell lymphoma. Progression at 46 mo. Disease free at 10 mo. |
| Bier-Laning et al. (1995)| NR      | Left posterior scalp | Multiple surgical excisions                                 | 10          | Primary site with dura involvement (cranectomy) | Debulking only + RT (54 Gy).                               | Right lower eyelid involvement at 13 mo salvaged with RT (60 Gy). Disease free at 7 mo. |
| Bier-Laning et al. (1995)| NR      | Right cheek        | Multiple surgical excisions                                 | NR          | Primary site + right CN Vb            | MMS with positive margin > surgical excision (right cheek, anterior wall of maxilla, infraorbital nerve) | Field edge recurrence at 18 mo, treated with reirradiation (45 Gy). Recurrence at 19 mo requiring multiple reirradiation + resections + chemo. Remained with suspicious lesion on lip. |
| Bier-Laning et al. (1995)| NR      | Right upper and medial cheek | Surgical excision                                           | 96          | Primary site                          | RT (60 Gy)                                                  | Field edge recurrence at 18 mo, treated with reirradiation (45 Gy). Recurrence at 19 mo requiring multiple reirradiation + resections + chemo. Remained with suspicious lesion on lip. |

Abbreviations: F – female, M – male, MMS - Mohs - micrographic surgery, NA - not applicable, NR- not reported, PNI - perineural invasion, RT - radiation therapy, TTR - time to recurrence, , NP – No progression
Table 2
Case reports of MAC of the head and neck treated with chemotherapy.

| Author (date)          | Age in years/Sex | Nature of recurrence | Primary site and nodal area | Primary treatment | Salvage treatment | Nature of recurrence | Outcome |
|------------------------|------------------|----------------------|----------------------------|-------------------|-------------------|----------------------|---------|
| Kim et al. (2020)      | 73/M             | NA                   | Surgical excision + RT     | RT + recurrence   | chemotherapy      | Recurrence at 8 mo   | No progression    |
| Haga et al. (2019)     | 78/F             | NA                   | Surgical excision + RT     | RT + recurrence   | chemotherapy      | Recurrence at 15 mo  | No progression    |
| Chaudhari et al. (2015)| 14/M             | NA                   | Surgical excision + RT     | RT + recurrence   | chemotherapy      | Recurrence at 8 mo   | No progression    |
| Bier-Laning et al.     | 46/F             | NA                   | Surgical excision + RT     | RT + recurrence   | chemotherapy      | Recurrence at 8 mo   | No progression    |

Abbreviations: F – female, M – male, NA - not applicable, NR - not reported, RT - radiation therapy, TP - tumor progression, PR - partial response, NP – No progression.

Despite the aggressive presentation, we treat each case considering age, health status, with exhaust treatment option to reach best local control and survival rate with utilizing available modality and treat the patient with best option. This particular case presented had experiences that warrants additional information on the limited resources on the management strategies of MAC. Also, this may pose as a model treatment modality to most likely similar cases. Nevertheless, close clinical follow-up and periodic self-examination are important to monitor locoregional, distant metastasis, as well as side effects in cancer treatment. Although the side effects of such treatment have significant impact on survivors’ quality of life, morbidity, and mortality. The long-term sequelae of the multiple modalities were discussed with and agreed by the patient prior treatment. Starting from locoregional side effects examination are important to monitor locoregional, distant metastasis. Additionally, variant courses of radiation therapy (RT) and chemotherapy offers excellent local–regional control for patients with skin adnexal carcinomas and risk factors for local regional recurrence.

4. Conclusion

Microcystic adnexal carcinoma (MAC) is a rare tumor with diverse histological patterns and a tendency for locoregional and distant metastasis. Surgical excision followed by adjuvant radiation therapy (RT) and chemotherapy offers excellent local–regional control for patients with skin adnexal carcinomas and risk factors for local regional recurrence.

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Availability of data and materials
Please contact author for data requests.

Consent for publication
Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.
Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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