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Case Report

Angiosarcoma of the Scalp: What is the Optimum Management?

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Abstract

Scalp angiosarcoma is a rare malignancy with a poor outcome. In the absence of randomized trials, the approach to management depends on retrospective series and case reports. Here, we report a 56-year-old male diagnosed initially with squamous cell carcinoma of the scalp at an outside center. When he underwent re-excision for recurrence in our center, histopathology showed a high-grade angiosarcoma. He was offered postoperative radiotherapy for the primary site. During the treatment, he developed preauricular nodal recurrence, which was also treated with radiotherapy. After radiotherapy, he had persistent preauricular nodes, for which single-agent chemotherapy was given, and the nodes were regressed. However, the recurrence of preauricular nodes was noted at the next follow-up visit, and he was re-evaluated with a positron emission tomography-computed tomography scan, which showed an extensive lung and nodal metastases. He was started on metronomic chemotherapy and his disease was stable at the time of the last follow-up. This case raises several questions, including whether electively addressing the regional nodes in the scalp angiosarcoma could improve the outcomes, whether higher doses of radiotherapy are beneficial or only add to the toxicity of treatment, the role that chemotherapy plays and the most appropriate regimen. Although some relevant studies have been discussed in brief, more evidence is needed to answer these questions.

Keywords: Angiosarcoma scalp, chemotherapy, metronomic, multimodality, radiotherapy, surgery

Introduction

Cutaneous angiosarcoma is a rare malignancy comprising <10% of head-and-neck sarcomas, which themselves comprise <1% of all head-and-neck tumors.[1] The most common presentation is a reddish-purple lesion over the scalp or face in elderly males, and it is often mistaken for ecchymosis, eczema, hemangioma, or other cutaneous conditions. The treatment mainly comprises surgery, adjuvant radiotherapy, and chemotherapy. Here, we discuss a postoperative case of angiosarcoma scalp treated with adjuvant radiotherapy and chemotherapy.

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Case Report

A 56-year-old male presented to our clinic with a 1-year history of scalp swelling. He had been treated surgically for a similar swelling 1 year back at another center. Histopathology showed a

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squamous cell carcinoma. Subsequently, he received six cycles of chemotherapy with cisplatin and five-fluorouracil (5FU) and was kept on followup.

The patient came to our center when he noticed the recurrence of the swelling. Clinically, there was a 2.5 cm × 2.8 cm hard reddish nodule on the right frontoparietal scalp adjacent to the postoperative site. A computed tomography (CT) scan showed a well-defined lesion in the scalp along the frontal region with no underlying bone erosion and no other metastases [Figure 1]. Following presurgical workup, he underwent wide local excision of the lesion. Initially, a nodal dissection was not planned, as he was clinically and radiologically node negative. Histopathology of the specimen revealed superficial and deep dermis infiltrated by a partly circumscribed tumor arranged in sheets and papillary structures. Vascular channels displayed slit-like lumina in areas, lined by atypical spindle to polygonal cells displaying moderately pleomorphic hyperchromatic nuclei, inconspicuous nucleoli, and scant-to-moderate amounts of cytoplasm. Occasional multinucleated tumor giant cells were also seen. The papillary structures and vascular channels showed multilayering of the lining epithelium. Foci of necrosis within the tumor were noted, and a few cells showed prominent cytoplasmic vacuolization. There was increased mitotic activity (~22/10 hpf), including atypical mitotic forms. The tumor encased a few nerve bundles and infiltrated underlying skeletal muscle fibers and adipose tissue. The tumor reached the undersurface of the epidermis, which also showed focal surface ulceration. The scanty intervening stroma showed aggregates of lymphocytes. The tumor was at a distance of 0.5 cm from the medial margin, 1.1 cm from the superior margin, 0.9 cm from the lateral margin and inferior margin, and 0.2 cm from the deep margin. Immunohistochemistry showed that tumor cells were positive for CD31 (membranous and cytoplasmic), FLI-1 (nuclear), focally positive for WT-1, and negative for CD20, CD56, CD34, and cytokeratin [Figure 2]. A histopathological correlation could not be done, as the patient did not have histopathology specimens from the initial surgery.

In view of the recurrent nature of the lesion and close margins, adjuvant radiotherapy was offered to the patient. Radiotherapy was planned to the postoperative bed with a margin of 4 cm all around followed by a boost to the postoperative bed with a 1-cm margin all around. Volumetric-modulated arc therapy (VMAT) was performed for the scalp lesion [Figure 3].

During radiotherapy, the patient developed preauricular swelling on the same side as the lesion. Fine-needle aspiration cytology was done from the lesion, which showed a metastatic malignant neoplasm. Subsequently, a separate nodal volume was contoured comprising bilateral superficial parotid nodes. A phase II nodal volume was also contoured comprising gross nodes. A VMAT plan was not considered for the nodes, as good coverage could be achieved with a three-dimensional conformal radiotherapy plan with minimal low-dose spill to normal tissues, which would have been difficult with a VMAT plan [Figure 4]. The scalp lesion was given 45 Gy in 25 fractions followed by a boost of nine Gy in five fractions. Nodal volume was given 45 Gy in 25 fractions followed by 14.4 Gy in eight fractions. All organs at risk constraints were achieved. The patient developed a maximum of Grade II dermatitis during radiotherapy and was managed symptomatically. He completed the treatment without any breaks.

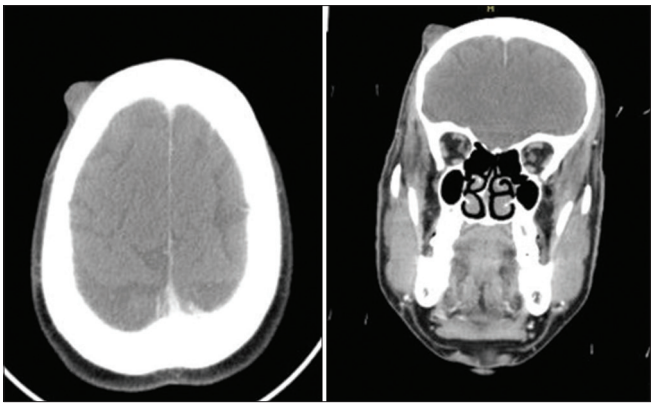

Figure 1: Axial and coronal views of a brain computed tomography scan showing a well-defined soft-tissue density lesion in the scalp along the right frontal region, measuring 16.5 mm × 11 mm, abutting the underlying bone with periosteal reaction. No features of intraparenchymal involvement were noted

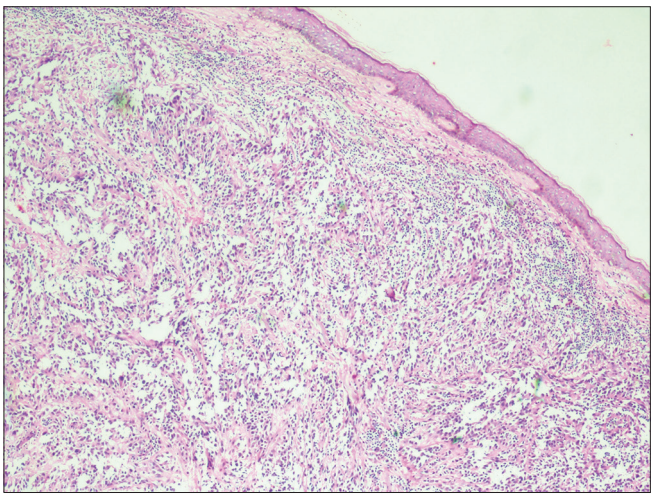

Figure 2: A tumor in the dermis with overlying skin (H and E; ×40)

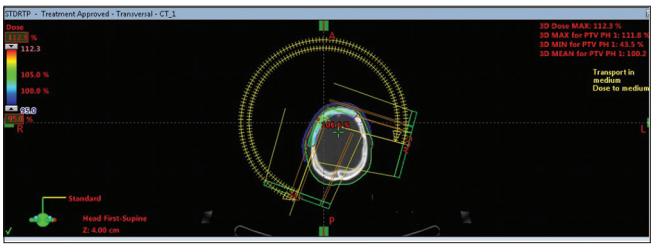

Figure 3: Volumetric-modulated arc therapy plan for the scalp lesion. Dose color wash showing 95% of dose distribution for planning target volume scalp

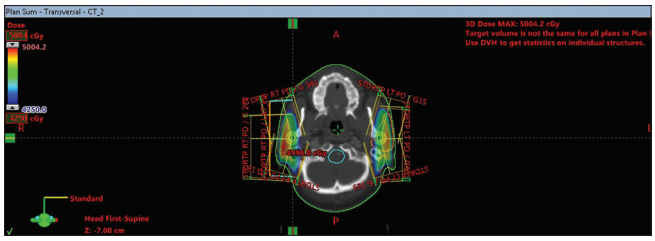

Figure 4: Three-dimensional conformal radiotherapy plan showing 95% dose distribution for bilateral preauricular nodal regions

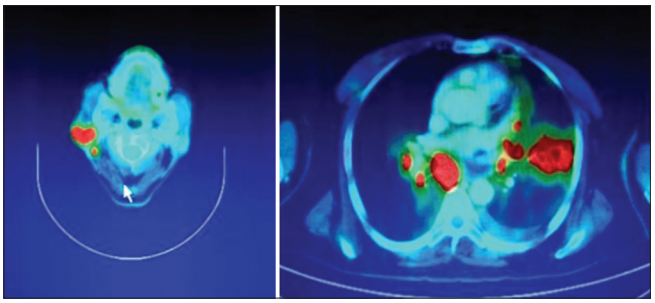

Figure 5: Axial positron emission tomography computed tomography slices showing extensive lung, mediastinal, and cervical nodal metastases

On the first follow-up, the patient complained of mild pain over the scalp. On examination, no recurrence was noted over the scalp, however, bilateral preauricular nodes persisted.

In view of nodal disease, single-agent adriamycin (the patient could not afford liposomal doxorubicin or paclitaxel) was started. He received four cycles of chemotherapy with significant regression of the nodes; however, further chemotherapy was withheld in view of dropping blood counts, pneumonia, and poor tolerance of the patient. At 2-month follow-up after the last chemotherapy, the preauricular swelling had again increased in size. The surgical removal of the node was planned, and a positron-emission tomography (PET)-CT scan of the whole body was done for presurgical evaluation. Unfortunately, the PET-CT scan revealed extensive metastases in the lungs and other neck nodes [Figure 5]. He was thus offered palliative metronomic chemotherapy with vinblastine, methotrexate, and propranolol. Eight months after the diagnosis of disseminated metastases, he was found to have disease regression on metronomic chemotherapy. However, he started having persistent low counts leading to treatment breaks, and thus vinblastine was omitted from the schedule. He was doing fine at last contact, which was 18 months after the first visit at our center and 27 months since the initial diagnosis at an outside center.

Discussion

Angiosarcoma is a fatal malignancy which often masquerades as a benign lesion in the initial stages, and this often delays the diagnosis. Chronic lymphedema and radiation exposure are known as predisposing etiologies. In a review by Naka *et al*.,[2] of 99 Japanese patients, factors such as chronic pyothorax for angiosarcoma of the pleural cavity and thorotrast exposure in liver angiosarcoma, were also found to be causative factors besides radiotherapy and chronic lymphedema.

Histopathologically, it can often be misdiagnosed as hemangioma or lymphangioma. Poorly differentiated lesions often mimic melanomas or epithelial malignancies, such as basal cell carcinoma or squamous cell carcinoma. Typically, a well-differentiated angiosarcoma comprises interconnected vascular channels with malignant endothelial cells protruding into vessels. Cytoplasmic and nuclear immunohistochemical markers used most frequently to establish the diagnosis are CD31, CD34, Erythroblast transformation specific related gene (ERG), and FLI1.[3]

In our patient, the lesion was initially reported as squamous cell carcinoma. The initial histopathology specimen was not available for review. However, the patient's demographics, location, and nature of the lesion were all suggestive that the initial lesion could have been angiosarcoma. In addition, as discussed previously, poorly differentiated angiosarcoma lesions can often be diagnosed as basal cell and squamous cell carcinomas. It is difficult to suggest that chemotherapy could have led to the origin of the angiosarcoma at the previous site of squamous cell carcinoma, as the author could only find one case report of splenic angiosarcoma in a follicular lymphoma patient treated with a long duration of chemotherapy. In addition, the time to the secondary angiosarcoma was relatively short compared to a reported latent period of at least 7–8 years.[4,5]

Considering the current evidence, multimodality treatment combining surgery and radiotherapy seems to be a reasonable approach; however, the role of chemotherapy still remains ill-defined.[6] For scalp angiosarcomas, wide local excision with a local flap after confirming negative surgical margins is the usual surgical technique. Nodal spread in angiosarcoma is higher compared to other sarcomas and has been reported to be almost up to 20%–30%.[7] The parotid nodal basin is the most commonly involved nodal region; however, the elective nodal dissection is not routinely practiced. Lim *et al*.[8] reported a case series of eight patients and found superior survival in patients who underwent wide local excision of scalp lesions with the removal of pericranium along with ipsilateral parotidectomy and upper neck dissection. All of their patients were reported to be disease free at 18 months after the surgery.

Adjuvant radiotherapy is used for all scalp angiosarcomas in view of the high propensity for the diffuse local spread and consequent high local recurrence. The curved surface of the scalp presents a challenge in the planning and delivery of radiotherapy. However, with the advent of newer techniques such as intensity-modulated radiotherapy, high doses can be delivered effectively while sparing normal tissues. In a postoperative setting, doses of 60 Gy–66 Gy are advocated, whereas in a definitive setting, 66–70 Gy is most commonly used. Suzuki *et al*.[9] reported that patients receiving a biological effective dose (BED) of >95 Gy in a definitive setting did better than those who received a BED <95 Gy. However, Grade IV complications were higher in the higher BED

group. Surface brachytherapy is another promising radiation delivery technique considering its excellent conformality. Sanada *et al*.[10] treated nine patients with scalp angiosarcoma with three fractions of 3 Gy per week using customized thermoplastic masks with applicators fixed *in situ* to avoid displacement and reported a 3-year overall survival rate of 50.8%. Local recurrence was significantly higher in the patients receiving <60 Gy, thus, they recommended doses ≥60 Gy in 20 fractions when using brachytherapy. Although with an aggressive malignancy such as angiosarcoma, it is difficult to predict the ultimate course of the disease. In our patients, higher doses of radiotherapy, especially for the gross nodes, could have possibly improved the outcome.

The need for elective surgery or radiotherapy for regional nodes in scalp angiosarcoma has still not been established due to a lack of sufficient evidence considering the rarity of this disease. However, nodal metastases portend a poor prognosis and are considered to be a harbinger of distant metastases. In our patient, nodes were not addressed electively and were planned for definitive radiotherapy on nodal recurrence. We postulate that upfront nodal dissection or elective nodal irradiation may benefit angiosarcoma patients.

Regarding chemotherapy-, adriamycin-, and paclitaxel-based chemotherapy regimens have shown benefits in isolated case reports and series of angiosarcoma. Other agents that have been used include liposomal doxorubicin, cisplatin, 5FU, and gemcitabine; however, all have shown limited benefits. Anti-vascular endothelial growth factor (VEGF) antibodies are also being explored, considering that VEGF plays a key role in the pathogenesis of angiosarcoma.[6] Limited evidence exists regarding the benefits of metronomic chemotherapy in angiosarcoma. Banavali *et al*. reported a study of seven patients with advanced, metastatic, and recurrent angiosarcoma treated with a combination of propranolol, methotrexate, and vinblastine. There was a 100% response rate with one complete response, and the median progression free and overall survival periods were 11 and 16 months, respectively.[11,12] In another report by Jiang *et al*.,[13] an 85-year-old female with recurrent scalp angiosarcoma was treated with metronomic cyclophosphamide and methotrexate after she stopped responding to the first-line agents. A complete resolution was achieved in the 3rd week of treatment and the response was sustained for 8 months, after which recurrence occurred at the primary site.

In a pilot study, using metronomic trofosfamide, celecoxib, and pioglitazone, Vogt *et al*.[14] reported a median progression-free survival of 7.7 months in six patients with recurrent or advanced vascular malignancies, of which five were angiosarcoma. In our patient, there was also a sustained response with metronomic chemotherapy for 8 months, which was the time of the last contact. These initial reports have shown promise in the use of metronomic chemotherapy in advanced angiosarcoma and pave the way for further research in this area.

To conclude, scalp angiosarcoma is an aggressive malignancy warranting aggressive and early treatment. In our patient, a more aggressive surgical approach including elective nodal dissection and higher doses of radiotherapy along with elective nodal irradiation may have contributed to a better outcome. The use of metronomic chemotherapy in our patient resulted in a significant regression of the disease and sustained response, which could be an area of further research. Treatment-related toxicities should also be considered when planning multimodality treatment.

Ethical statement

This research work was exempted from the Institutional Review Board Review of CMC, Vellore, as appropriate patient consent was obtained from the patient, and this was a noninterventional research work.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient have given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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