Angiosarcoma of the of Scalp with Calvarium Involvement in a 50-Year-Old African-American Man

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Background: Angiosarcoma of the scalp is a rare, aggressive, and deadly cancer that affects mainly elderly Caucasian men.

Objectives: The insidious and masquerading presentation of angiosarcoma poses enormous diagnostic challenges for primary care providers.

Patients/Methods: We present a case of a 50-year-old black man referred for evaluation of a 3.7-cm-x-5.4-cm ulcerated, fluctuant scalp lesion that had failed to respond to different antibiotics and proper wound care.

Results: Surgical excision and subsequent histopathology revealed angiosarcoma.

Conclusions: This case report highlights the importance of high index of suspicion for early diagnosis of cancerous lesions in wounds and stresses the need to include angiosarcoma in the differential diagnosis for all face and scalp lesions, as early detection may save lives. A comprehensive literature review is also presented.

Key words: angiosarcoma ■ black ■ head and neck cancer ■ scalp

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INTRODUCTION

Angiosarcoma is an extremely malignant soft tissue sarcoma of endothelial origin. Because of its ambiguous presentation that usually mimics common benign dermatologic conditions, it is often diagnosed late.[1-5] These sarcomas account for about 1% of all sarcomas and less than 0.1% of all head and neck cancers.[6,7] Therefore, the rarity of angiosarcoma may impede early diagnosis. Radiation and chronic lymphedema have been implicated in the development of some cutaneous angiosarcomas.[4,5,8-13] Angiosarcoma is usually found in elderly Caucasian men in their 70s.[1-5] Angiosarcoma has the highest rate of lymph node metastases of all soft-tissue sarcomas of the head and neck, and distant metastasis may occur in up to 50%, with the lung being the most common site.[1-5,7,14-17] Prognosis is dismal regardless of histologic type and therapy.[3-5] Age, patient's sex, location, and clinical appearance have no effect on prognosis.[1-5] However, tumor size has been found to correlate with favorable outcome,[3-5] hence, the need for early diagnosis and aggressive management. The overall five-year survival rate is less than 30%.[2-5,11,18-20]

We present a case of angiosarcoma in a 50-year-old African-American man who presented to our clinic with a nine-month history of a slow-growing lesion on the right occipitoparietal area of the scalp.

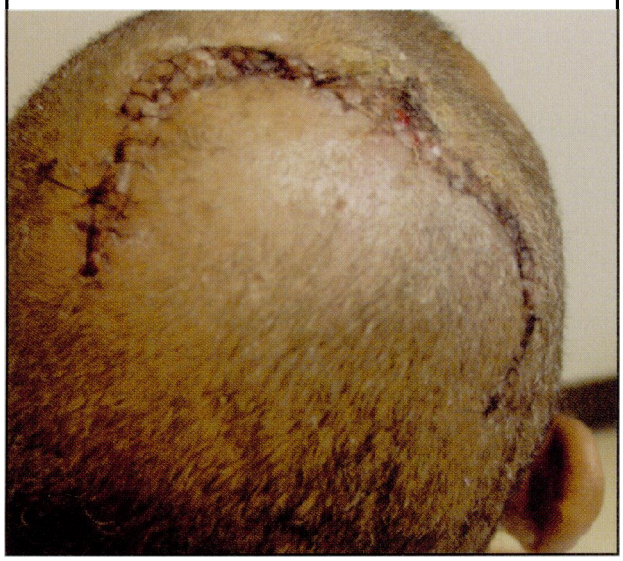
CASE REPORT

A 50-year-old African-American man related a nine-month history of a scalp "knot" that measured about 1 cm x 0.5 cm. He scratched the lesion repeatedly, leaving him with an enlarging ulcer. Three weeks later, he presented to his primary care physician because of the foul smelling nature of the lesion. He was initially treated with antibiotics for seven days but with no resolution. He was again seen about two weeks later and was prescribed another regimen of antibiotics for 14 days. The lesion continued to increase in size associated with fluctuance and pruritus. The patient returned a third time and was given a 21-day course of antibiotics along with instruction to clean the lesion

four times daily. By this time, the lesion had become an ulcerated mass. He was eventually referred to a dermatologist eight months after the lesion was first noticed. A biopsy of the lesion revealed atypical vascular proliferation that resembled granulation tissue but with focal atypical features including papillary formation and dissection in between the reticular collagen bundles. A few nonatypical mitotic figures were also noted associated with a marked mixed inflammation. Given the age and race of the patient in conjunction with the history, the dermatopathologist favored pyogenic granuloma as the top differential. Others on the differential included deep fungal infection, granulomatous inflammation, squamous cell carcinoma, and basal cell carcinoma. The patient was then referred for surgical evaluation. On physical exam, a fluctuant fungating and foul-smelling mass measuring 3.7 cm x 5.3 cm was noted in the right occipitoparietal area with purulent drainage. No cervical or posterior auricular lymph nodes were palpable, and the rest of the physical exam was otherwise unremarkable. Nine months after the patient first noticed the "knot", the mass was excised with primary closure (Figure 1). The excised tissue was submitted for surgical pathology consultation.

The specimen submitted was an ellipse of hairy skin measuring 8.3 cm x 4.6 cm x 1.7 cm with a central well circumscribed 2.8 cm x 2.7 cm necrotic red-tan area that extended to within 0.1 cm to the deep resection margin. Histopathologic examination by light microscopy showed skin ulceration with superficial necrosis and bacterial colonies within the necrotic tissue debris (Figure 2A). Beneath the ulcer exudate, the lesion comprises a vascular proliferation that resembled granulation tissue with chronic inflammation (Figure 2B). Destruction and replacement of skin adnexal structures were also noted along with presence of abnormal vascular architecture, interconnections between the vascular channels, and dissection through collagen bundles (Figure 2C). High magnifications showed rather large and occasionally bizarre-looking pleomorphic atypical cells with hyperchromatic nuclei, and high nuclear-cytoplasmic ratio lined the vascular channels. Rare mitotic figures were also detected (Figures 2D, 3A). The tumor was also present at the deep margin of the excised lesion, but the radial surgical margins were all free of tumor. Postoperative CT scan of the head and MRI of the brain revealed invasion of the underlying parietal bone through its entire thickness over an area that measured about 3.5 cm in diameter, but the underlying brain was not involved (Figures 3B, 4A, 4B). Consequently, the patient was taken back to the OR for craniotomy and excision of the involved calvarium with metal capping (Figure 5). Immunohistochemistry confirmed the endothelial origin of these tumor cells by their diffusely strong immunoreactivity with markers for endothelial cells (Factor VIII-Related Antigen and CD31) (Figure 3C). CT of the chest, abdomen, and pelvis did not reveal metastases. The patient is currently receiving radiation and chemotherapy.

Figure 1. Primary closure after excision of the lesion (POD #7).



DISCUSSION

Angiosarcoma of the scalp is a rare and deadly malignant tumor classically found in elderly Caucasian males.[1-5] It was first described by Livingston and Klemperer in 1926, when they reported a tumor of the scalp in a 38-year-old white male who later died from uncontrolled hemorrhage from the tumor.[21] E. Wilson Jones, 38 years after the first case was published,[1,22] described a series of nine cases occurring on the face and scalp of elderly patients.

These tumors are more commonly found in the elderly with the mean age of presentation from 68–76 years.[1-5,19,23] The male-to-female ratio is roughly 2:1.[1-5,14,19,23] They account for 1% of all sarcomas and less than 0.1% of all head and neck cancers.[6,7] These tumors may be found in any location, although they have a predilection for the skin and superficial soft tissues in sharp contrast to most other sarcomas that are usually located deep within the body.[6,24,25] Of those occurring on the skin and superficial soft tissue, over 50% are found in the head and neck region.[6,24] In reference to the head and neck region, these lesions are frequently found in the upper half of the face or scalp.[3-5]

The rarity and masquerading presentation of angiosarcoma often lead to late diagnosis. Common presentations in the literature include induration, erythematous nodules, bruise-like plaques, fungating masses, ulcerations, alopecia, violaceous nodules, macules, and bleeding wounds.[1-6,22,24-32] While the ulcerated and hemorrhagic lesion suggests a more-advanced stage of angiosarcoma, the indurated and plaque-like

lesions are more indicative of poorly differentiated and moderately differentiated tumor, respectively.[1-3,14,19]

The aggressive nature of angiosarcoma is evident by frequent local invasion into the underlying calvarium and even brain invasion.[2,4,5,14,33-35] Distant metastases occur up to 50%, via hematogenous as well as lymphatic route.[1-5,14] The lung is the most common site of distant metastasis, followed by the liver.[1-5,14-17]Other reported sites of metastases include heart, spleen, intestines, retroperitoneum, bone, bone marrow, and kidney.[3,14-16] Delayed recurrence of angiosarcoma at distant sites has been reported, making regular lifelong surveillance paramount.[3-5,14,36,37] The highly metastatic nature of this tumor has been postulated by Tanioka and colleagues to be due to the absence of vascular endothelial cadherin (VE-cadherin), which is present in normal endothelium.[32]

There are no delineated risk factors for this deadly cancer, but chronic lymphedema, which was first reported by Treves and Stewart, and prior radiation exposure have been linked to angiosarcoma.[4,5,8-13,38] McConnell and associates suggest connective tissue dystrophy caused by persistent, chronic lymphedema may be the inciting factor for the genesis of angiosarcoma.[38] Also, the concept of connective tissue damage has been postulated by several based on the occurrence of angiosarcoma in adult patients who received radiation during infancy.[11-13,39] Sun exposure and consequent actinic skin damage was once proposed to be associated with the development of angiosarcoma due to its rarity in blacks and overt predominance in Caucasians.[3,11,12] But this theory has been refuted by other reports that showed most of the patients with angiosarcoma of the scalp had hair, affording protection to the affected sites.[2-5] Trauma was also considered but not substantiated as an inciting agent for the development of angiosarcoma.[1,36,40] Reed and colleagues, who reported a series of six cases in whom five had a history of minor trauma, concluded that the trauma may have "merely alerted the patient to the presence of the tumor rather than having served as a causative agent."[36] Other predisposing factors that have been cited in individual cases include occurrence of tumor at former herpes zoster sites, complication of telangiectating nevus, other vascular and lymphatic abnormalities, and fistula complicating chronic osteomyelitis.[10,36,39,41-45] In other reports, including the two largest series of angiosarcoma affecting the face and scalp, no underlying predisposing factors were found.[3,4]

The treatment of this dreadful, unrelenting sarcoma includes surgical excision with wide margins, radiation therapy, immunotherapy, and chemotherapy. A combination of any of these forms of treatment can be used with some success. With the exception of wide surgical excision, no single treatment modality has proven to be effective.[1-5,10,14,17,46-52] Suc-

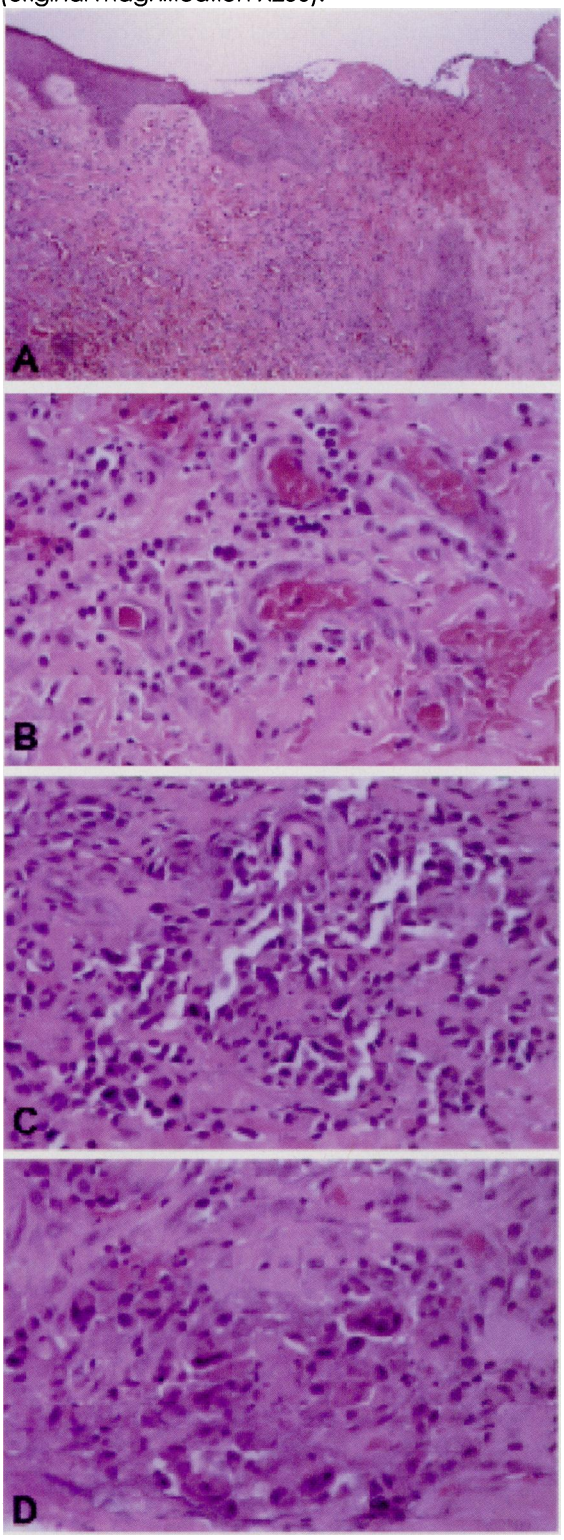
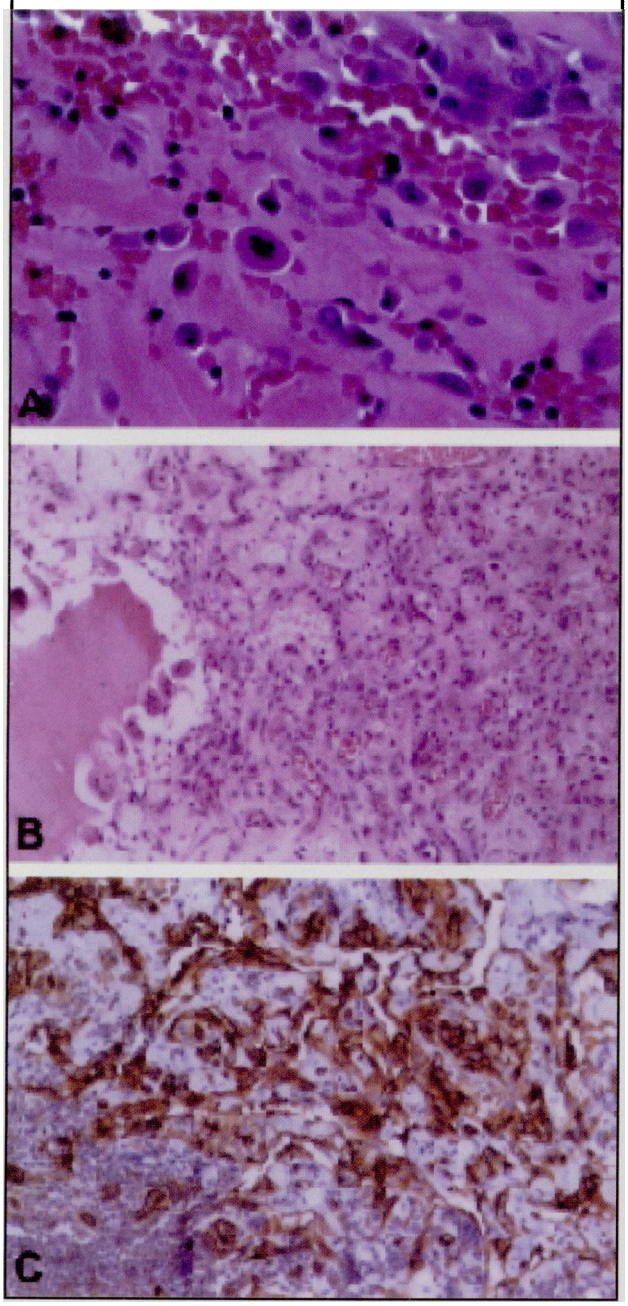


Figure 2. A. Skin ulceration with subjacent granulation tissue (original magnification X40). **B.** High power of A showing granulation tissue with mononuclear chronic inflammatory cells (original magnification X250). **C.** Vascular channels dissecting through collagen (original magnification X250). **D.** Atypical cells lining the vascular channels (original magnification X250).

cessful treatment with recombinant interleukin-2 (rIL-2) has been reported.[26,32,50-52] Ulrich and associates advocate intralesional cytokine therapy alone or in combination with surface irradiation as an alternative therapy for nonsurgical candidates.[51] Liposomal doxorubicin has been given with some success.[53]

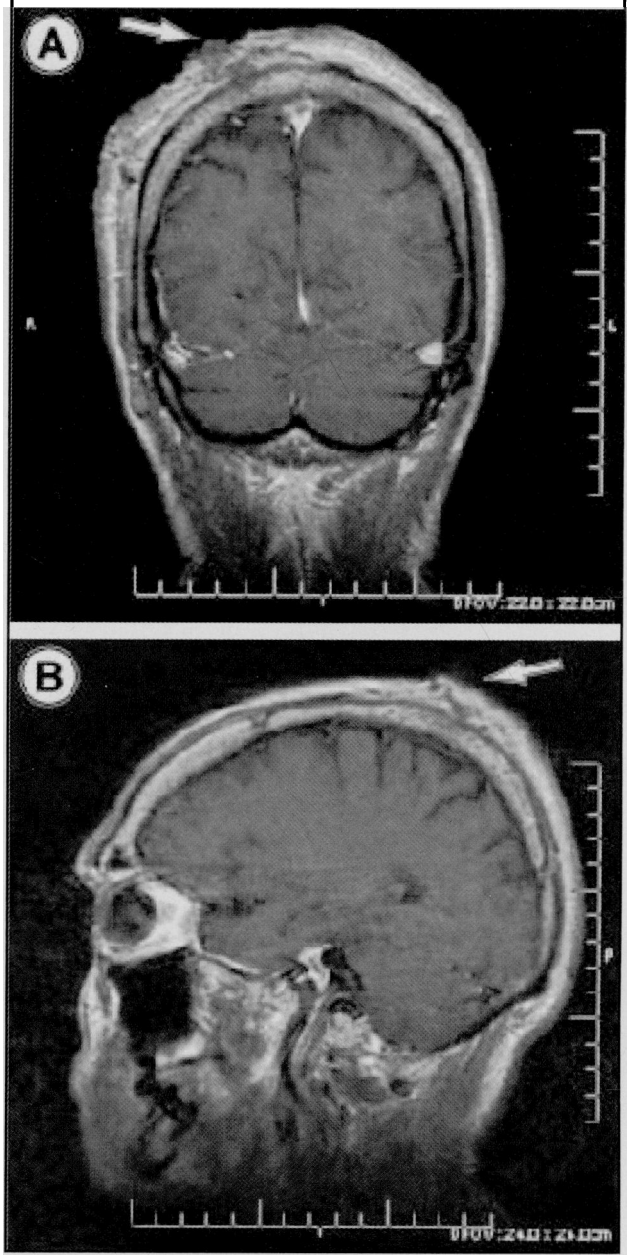
Figure 3. A. Atypical endothelial cells with hyperchromatic nuclei and an atypical mitotic figure in the center (original magnification X400). **B.** Lesion with granulation tissue-like appearance invading the calvarium (original magnification X100). **C.** Diffuse and strong positive staining reaction with antibody against CD31, a marker for endothelial cells (original magnification X100).



Radical electron-beam therapy of small lesions using wide fields affords the best opportunity of eradicating cutaneous lesions.[3,11]

The overall prognosis of angiosarcoma is grim. It is an aggressive tumor with a high propensity for both local occurrence and distant metastases. The single most important prognostic factor is the size of the lesion at the time of presentation, making early diagnosis crucial.[3-5] The histologic differentiation of the tumor has no effect on prognosis.[2-5] However, a marked lymphocytic response and lack of appendageal destruction by the

Figure 4. A. T1-weighted MR image showing tumor invasion through the outer table into the diploic portion of the skull, **A.** Coronal view and **B.** Sagittal view.



tumor have been associated with a better prognosis.[5,54] Factors like age, sex of the patient, the location of the lesion (scalp vs. face), and the clinical appearance of the lesion have no statistically significant effect on the prognosis.[3-5] The only statistically significant predictor of prognosis is tumor size at initial presentation.[3-5] Lesions smaller than 5 cm have been shown by different groups to significantly increase the probability of survival.[3-5] Some series reported a five-year survival of less than 10%.[2,40] Others, including some of the biggest reviews up to date, cite a five-year survival of less than 30%.[2-5,19,20,23] In the UCLA review, they reported 50% of the patients dying within 15 months.[4] Maddox and colleagues reported a median survival of 20 months.[5] In a recent review of prognostic factors for soft-tissue sarcomas using a relatively large database (1,240 patients), the following were found to be statistically significant independent predictors of subsequent metastasis: tumor size, tumor grade, neurovascular or bone involvement, and tumor depth.[55] All of these factors, with the exception of tumor grade, are dependent on the tumor size. Hence, the need for early diagnosis and aggressive management with tumor excision cannot be overemphasized.

CONCLUSION

Angiosarcoma carries an inevitable mortality if not diagnosed promptly. No single treatment modality is efficacious if the diagnosis is delayed. A tumor size of less than 5 cm is associated with a better prognosis, making early detection important. When feasible, wide surgical excision is advocated with subsequent radiation therapy. Because of the tumor's propensity for local recurrence and distant metastases, even after a prolonged disease-free state, life-long surveillance, especially pulmonary surveillance, is strongly advised. To the best of our knowledge, this is the fourth reported case of angiosarcoma in a black individual, and the youngest patient with no prior history of irradiation or chronic lymphedema.[56] We urge that general physicians become familiar with this devastating cancer, since early and prompt intervention allows the greatest opportunity for cure.

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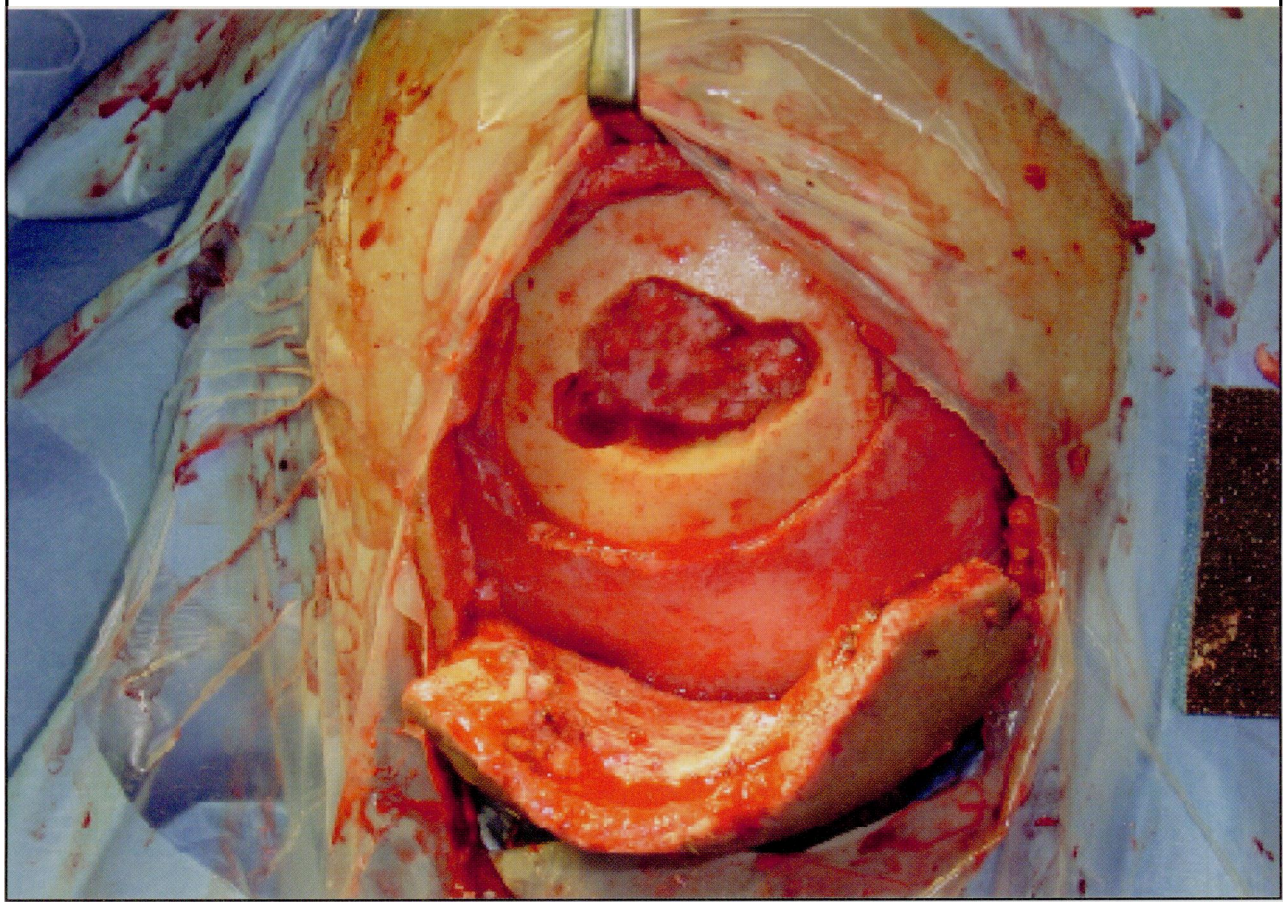
Figure 5. Intra-operative photograph showing excision of the involved calvarium.



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