# Hematological Paraneoplastic Syndrome and Heparin-Induced Thrombocytopenia in Untreated Parotid Acinic Cell Carcinoma - A Case Report

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## Abstract

**Rationale:** Acinic cell carcinoma (ACC) is a rare and indolent malignancy commonly found in the parotid gland. This can give rise to paraneoplastic syndromes, which represent the clinical manifestations of indirect and remote events produced by tumour metabolites. **Patient Concerns:** A 38-year-old Afro-Caribbean female suffered an indolent parotid mass. She only presented to our tertiary center when it started to ulcerate and bleed. **Diagnosis:** She was diagnosed with advanced parotid ACC. She also went on to develop an hematological paraneoplastic syndrome resulting in venous thrombi. This was complicated by her developing heparin-induced thrombocytopenia (HIT). **Treatment:** A difficult multidisciplinary decision was made to proceed with surgery despite her extremely poor condition. **Outcomes:** After the surgery, the patient made a full recovery. **Take-away Lessons:** ACC is a relatively uncommon and indolent malignancy that is usually found in the parotid gland. It can be associated with a hematological paraneoplastic syndrome and further complicated by iatrogenic HIT.

**Keywords:** Heparin-induced thrombocytopenia, malignancy, parotid, thrombosis

## Introduction

Acinic cell carcinoma (ACC) is a relatively uncommon and indolent malignancy of the parotid gland. It shows a female predilection and is most frequent in the fifth decades of life.[1] Diagnosis is with fine-needle aspiration and treated with surgical excision and adjunct radiotherapy.

Paraneoplastic syndromes are the clinical manifestations of underlying malignancy. Paraneoplastic syndromes can be more serious than the consequences of the primary tumour itself and can cause significant problems in the management of these patients. We present a patient with neglected advanced parotid ACC, its hematological paraneoplastic syndrome, and the subsequent therapeutic complication.

## Case Report

### Patient concerns

A 38-year-old Afro-Caribbean female presented to the otolaryngology outpatient clinic with bleeding from an ulcerating left fungating parotid tumour. She first noted a pea-sized mass 5 years prior. A fine-needle aspiration cytology of the mass at that time showed ACC. The patient refused surgery and was lost to follow-up. The tumour slowly increased in size but within the last year underwent rapid growth.

### Diagnostic aids

She appeared malnourished and focused examination revealed a 14 by 12 cm fungating parotid mass with areas of necrosis and haemorrhage [Figure 1]. The motor function of the facial nerve could not be assessed properly due to the mass effect of the tumour.

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On admission, her hemoglobin was 9.3 g/L and albumin level <10 g/L. Other blood tests including electrolytes, liver function tests, and coagulation profile were normal.

## Treatment

The patient was admitted for nutritional support, hemostasis, and further management of her parotid malignancy.

## Outcomes

On the second day of admission, she developed acute confusion and became agitated. Computed tomography of the brain surprisingly showed a thrombosis of the contralateral transverse sinus extending into the proximal part of the internal jugular vein [Figure 2]. A Doppler ultrasound scan of the lower limbs revealed thrombosis of the distal part of the right common femoral vein. Following the advice from neurologists and hematologists, the patient was started on warfarin for anticoagulation. An inferior vena caval filter was also inserted to prevent thromboembolism from the femoral vein thrombosis.

On the 12$^{th}$ day of admission, the International Normalized Ratio (INR) value went up to 8.0, and the patient bled from the tumour site. Warfarin was stopped, and the patient was given Vitamin K and fresh-frozen plasma. Within the next 3 days, the INR came down to 2.0. Due to difficulty maintaining INR values within the therapeutic range, warfarin was switched to low-molecular-weight heparin (LMWH).

On the 28$^{th}$ day of admission, 8 days after starting heparin, the platelet count dropped from 500 to 15 × 10$^{9}$/L. The serum was positive for platelet factor-4 antibodies and a diagnosis of Type II heparin-induced thrombocytopenia (HIT) was made. The heparin was therefore switched to lepirudin, a direct thrombin inhibitor. The platelets returned to the normal level after 5 days of stopping heparin.

Three days later, the patient's condition deteriorated rapidly due to septicemia. She was transferred to the intensive care unit and started on broad-spectrum antibiotics. The patient's nutritional status got worse since her hospital admission as she was not having adequate per oral intake and refused nasogastric feeding.

Because of the patient's worsening prognosis despite maximal medical management, the multidisciplinary team recommended the surgery as a possible solution in addressing the primary issue, the tumour.

She underwent a radical left-sided parotidectomy and type-1 modified radical neck dissection, as the carcinoma was staged as T4, which has a high risk of having lymph node metastasis. Moreover, the neck dissection was necessary for facilitation of the latissimus dorsi pedicled muscle flap reconstruction. The facial nerve was sacrificed as the tumour engulfed all branches of the nerve, but the accessory nerve and internal jugular vein were preserved. A part of the zygomatic arch was also removed as the tumour involved it. Intraoperatively, the tumour was found herniating into

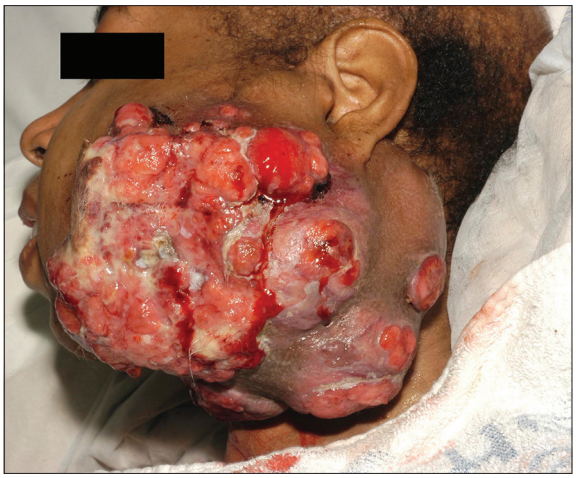

**Figure 1:** Massive fungating parotid tumor

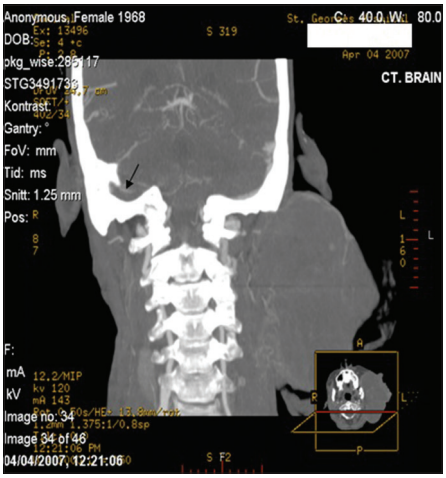


**Figure 2:** Right transverse sinus thrombosis (arrow showing the absence of contrast)

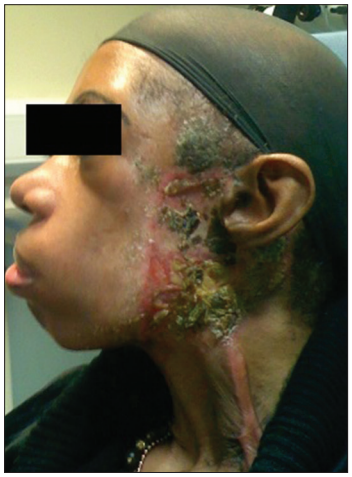

**Figure 3:** Postoperative photograph taken 8 months later

the oral cavity through the parotid duct opening (Stensen's duct). The oral mucosa around the tumour was excised and closed primarily. A latissimus dorsi pedicled muscle flap was raised to reconstruct the facial defect and a split skin graft was used to cover the muscle flap.

The histology confirmed moderately differentiated ACC of the parotid with clear margins but noted vascular invasion. None of the 61 lymph nodes harvested were positive for malignancy. The disease was staged as pT4pN0M0.

### Follow-up

The postoperative complications included hematoma formation at the latissimus dorsi flap donor site, which was drained. The patient also developed an episode of septicemia due to an infected central venous catheter, which was treated with antibiotics. Part of the split skin graft had to be re-grafted due to a local wound infection.

After being an inpatient for 65 days, she was discharged from the hospital with a normalized serum albumin level and underwent adjuvant postoperative radiotherapy. There were no signs of any local or regional disease after her treatment [Figure 3]. Unfortunately, she died 19 months after the surgery due to lung metastasis.

## Discussion

Patients with parotid ACC commonly present with a slow-growing painless mass. One case series reported that only 7.5% reported pain and only 3.0% had facial nerve palsy.[2] Because of this, some patients may have waited 5–10 years before seeking help.[2] Macroscopically, the typical ACC is a solitary, well circumscribed, gray-white soft mass.[3]

The primary treatment of low-grade ACC is local excision. For high-grade tumours, the treatment involves wide local excision, selective neck dissection, and adjuvant postoperative radiotherapy.

Paraneoplastic syndromes can accompany malignant disease. Venous thromboembolism is a common occurrence in cancer patients due to the increased hypercoagulable state. The principal mechanisms are through the direct activation of blood clotting or through the activation of host cells. In the former, there is an increase in coagulation factors and a decrease in fibrinolysis. In the latter, procoagulants such as endothelial cells, platelets, and leukocytes are activated through soluble mediators such as inflammatory cytokines (interleukin-1 and tumour necrosis factor alpha) and surface adhesion encouraged through the upregulation of adhesive molecules (vascular cell adhesion molecule and intercellular adhesion molecule).[4]

If the only patent ipsilateral internal jugular vein was sacrificed, our patient would have had a five-fold increase in intracranial pressure leading to severe cerebral edema which has a high mortality rate perioperatively.[5]

The incidence of HIT is very variable and depends on which formulation of heparin is used (unfractionated heparin or LMWH) and the dosage (prophylactic vs. therapeutic).[6] Patients with HIT usually experience a platelet count drop of at least 50%, often to <150 × 109/L, typically happening 5–14 days postcommencement of heparin.[7] Even though HIT is associated with thrombocytopenia, bleeding is rare and instead it is strongly associated with thrombosis.[8] When HIT is suspected, all forms of heparin must be avoided, including LMWHs, heparin flushes, heparin-coated catheters, and an alternative anticoagulation must be initiated immediately.[9] No platelets should be transfused, and patients will need to be treated with warfarin for 3 to 6 months after the platelets recover. The warfarin will need to be bridged as it can increase the risk of microvascular thrombosis by affecting the natural anticoagulants such as protein C and S.[10]

## Conclusion

The management difficulties faced in this case included malnutrition, a hypercoagulable state leading to thrombi, septicemia, and HIT. Surgery was delayed for 4 weeks to optimize the patient for surgery. After the primary source of the patient's problems (the parotid tumour) was removed, the other difficulties resolved.

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### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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