PART I: METASTATIC BASAL CELL CARCINOMA

Introduction
Basal Cell Carcinoma (BCC) is the most common malignancy worldwide, with a lifetime risk of 30% in Caucasian, North American populations. It is generally an indolent skin tumour with low metastatic potential and high cure rates. However, consequences of metastasis are often deadly and it is important to be aware of this severe complication.

Clinical Presentation
There are 5 main clinical subtypes of BCC:

1) Nodular BCC- the most common variant presents as a firm, translucent papule or nodule with a smooth surface, telangiectasia, and well-defined borders. A cystic variant is uncommon.

2) Ulcerating BCC- also known as rodent ulcer, presents as an ulceration on the skin with a rolled border, translucency, smooth surface, telangiectasia, crusting.

3) Morpheaform/Sclerosing BCC- resembling a superficial scar, white/yellow waxy sclerotic plaque with pepperish pigmentation.

4) Superficial BCC- thin, erythematous plaques with telangiectasia and scaling. Usually multicentric.

5) Pigmented BCC- A rare variant, presents with black or brown macules superimposed on features of nodular BCC.

Most BCC’s occur as an isolated single lesion on the head and neck in light-skinned males over 40. Differential diagnosis of BCC include squamous cell carcinoma, actinic keratosis, sebaceous hyperplasia, dermatofibroma, superficial spreading and nodular melanoma, and melanocytic nevi, depending on its subtype.

Table 1: Predisposing factors for BCC

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<td>Skin phototypes I, II or albino with prolonged sun exposure</td>
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<tr>
<td>History of heavy sun exposure in childhood</td>
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<tr>
<td>X-ray therapy for facial acne</td>
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<td>Ingestion of arsenic (Superficial multicentric BCC)</td>
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<td>Immunosuppression</td>
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<td>Positive family history of skin cancer</td>
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<tr>
<td>Genetic conditions (albinism, xeroderma pigmentosum, Bazex’s syndrome, Gorlin’s syndrome)</td>
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BCC may be treated surgically or non-surgically. Surgical treatment includes electrodessication and curettage, cryosurgery, excision and Mohs’ micrographic surgery. The latter is reserved for cases in high risk sites.
on the face, morphoeic and recurrent tumours. Cure rates for surgical treatments exceed 95%. Non-surgical treatments are less effective and include radiation, photodynamic therapy, and topical fluorouracil or imiquimod.\textsuperscript{1,5}

**Metastasis**

Metastasis is such a rare occurrence that some sources even state that BCC does not metastasize. However, reported rates of metastasis range between 0.0028 to 0.55% of all BCC’s. Metastatic BCC (MBCC) was first described in 1849 by Beadles whose 46-year old male patient had an ulcerating BCC on the face metastasizing to the submaxillary lymph node.\textsuperscript{3} In 1951, Lattes et. al. described criteria for MBCC (Table 2):

Table 2: Lattes’ criteria for MBCC\textsuperscript{3}

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<td>Primary tumour originated from the skin and not from mucous membranes or other glands</td>
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<td>Metastasis occurred to a distant site from the primary tumour and could not result from direct extension</td>
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<td>Both metastatic and primary tumours have identical histopathology</td>
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Since 1849, there have since been only over 300 cases of MBCC reported. Many of the predisposing factors for MBCC are similar to those of BCC, commonly presenting in light-skinned individuals, males, and in the head and neck area. BCC’s have been found to metastasize through both hematogenous and lymphatic avenues, lymphatics being more common. Common sites for metastasis (in order of frequency) include lymph nodes, lungs, bones, skin and parotid glands. In von Domarus et. al.’s review of over half of these cases, patients first developed BCC at a median age of 45, and later presented with MBCC at a median age of 59.\textsuperscript{4} This is higher than that of BCC, and possible explanations include inherent aggressiveness of earlier-presenting BCC, or older patients may not survive to metastasis.\textsuperscript{3} Median time from start of BCC to progression to MBCC was found to be 9-11 years, but intervals range from months to decades.\textsuperscript{3} Prognosis of MBCC is poor, with a median survival of 8-14 months after its diagnosis, and a 5-year survival rate of 10\%\textsuperscript{3,4}

Table 3: BCC at high risk for metastasis\textsuperscript{3,4}

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<tr>
<td>Located on head and neck</td>
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<td>Size $&gt;$10cm</td>
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<td>Deeply penetrating tumours</td>
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<tr>
<td>Perineural spread</td>
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<tr>
<td>Invasion of blood vessels</td>
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<tr>
<td>Multiple recurrences in primary tumour site</td>
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<td>Morpheaform and adenocystic subtypes</td>
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Workup for patients with suspected MBCC consists of history and physical examination, concentrating on lymph nodes near the primary BCC. Helpful lab tests include CBC, liver function, bone scan, and CT scan of the chest, abdomen and pelvis.\textsuperscript{4}

Because of the rare nature and poor prognosis of MBCC, there is not much evidence surrounding optimal treatment. In general, treatment is palliative and depends on the location of metastasis as well as the general health and age of the patient. In cases of local spread, surgery provides the best prognosis, whereas radiation therapy and chemotherapy with Cisplatin is best for generalized disease.\textsuperscript{4}

**Conclusion**

Basal cell carcinoma is an extremely common malignancy that is sometimes treated by family physicians due to ease of treatment, however, knowledge of its deadly metastatic potential is crucial to prompt referral, treatment and possibly better prognosis for the patient.

**PART II: HYPERTENSION CAUSED BY A PHEOCHROMOCYTOMA AND IT’S MANIFESTATION IN PREGNANCY**

**Introduction**

Hypertension is a frequent complication of pregnancy and may compromise fetal and maternal outcome. Hypertension may be pregnancy-induced, essential or secondary to endocrine disorders. Most cases of endocrine hypertension are the consequence of adrenal diseases.\textsuperscript{3} In one case in the literature, a pregnant female who has been
suffering from persistent hypertension arrives at her family physician complaining of a headache. The patient is a recent immigrant to Canada and does not speak English very well. The results of the tests made during that visit find that the patient has a constellation of negative signs and symptoms: persistent hypertension, hyperreflexia, edema, proteinuria, oliguria, hyperuricemia and thrombocytopenia. The family doctor suspects preeclampsia. However, in this case the patient was eventually found to have a very rare condition called a pheochromocytoma.1

The most hazardous form of endocrine hypertension during pregnancy is a pheochromocytoma because it may involve paroxysmal arrhythmia and/or hypertension during labor.2 It is therefore important that it be diagnosed early during the pregnancy to reduce mortality and morbidity to the mother and the baby. Diagnosis is difficult however because a pregnant woman can present solely with chronic hypertension and headaches, which can lead one on the path to suspect preeclampsia or essential hypertension. In the case study, as the authors mention, the worsening headaches and labile hypertension could also be attributed to stress, cultural isolation and medication.3

Natural History

A pheochromocytoma is rare, found in about .01-.1% of patients with hypertension in the general population. There are only about 200 cases reported of it occurring in pregnancy.4 They are catecholamine secreting tumours of the adrenal medulla’s chromaffin cells (of neural crest origin and secreting epinephrine, norpinephrine and dopamine). They can occur at all ages in both sexes, but should especially be suspected in patients presenting with poorly controlled hypertension at less than 40 years of age.

In pregnancy, the maternal mortality rate is 2-4% if tumour is diagnosed in the antenatal period, and 14-25% if diagnosed intrapartum or after delivery.1 Fatal crises can be caused by various stimuli from anesthesia to the mechanical effects of vigorous fetal movement to the expulsive forces of vaginal delivery.4 Fetal mortality is 11-15% antenatally, but 55% if during labour or after delivery. 1

Pathophysiology

They are sporadic in 90% of cases and inherited in 10%. They are associated with MEN, MENIIA and MENIIB syndromes.1 They are often described by the 10% rule: 10% arise in association with familial syndromes, 10% are extra-adrenal, 10% in sporadic cases are bilateral, 10% are multiple and 10% are malignant. Prognostic factors for a pheochromocytoma include stage, age, histology, and various chromosomal markers such as DNA ploidy, n-myc amplification, trk- a expression, 17q gain, 1p loss and telomerase expression.

Diagnosis

Diagnosis is made by recognizing the effects of a hormonal milieu caused by excess catecholamine secretion (a sympathetic response) as well as the resulting production of various vasoactive peptides. A patient can present with a combination of hypertension, Headache, Hyperhydrosis (sweating flushing of the skin), Hypomotility of gut (constipation), hyperglycemia and hypermetabolism (tachycardia, anxiety, nausea, palpitations).

Also distinguishing is postural hypotension and hypertension worsening in the supine position.1 It can be sustained or paroxysmal, and there can be a drop in orthostatic blood pressure. Classical symptoms of pheochromocytoma can be reproduced by an abdominal massage in the postpartum period.1

A 24 hr urine screen for metabolites of catecholamines (metanephrines, fractionated catecholamines and vanillylmandelic acid) is the common screening test. A plasma screen can also be done for catecholamines or metanephrines. Two normal tests of plasma and urine catecholamines can exclude a diagnosis. Tests for tumor location are limited to ultrasound and magnetic resonance scans in order to avoid maternal and fetal irradiation.3

Differential

Other conditions which increase catecholamines include anxiety, pain, bladder distention, trauma and pressure on the tumor. Cardiomyopathy has been reported as a complication of a pheochromocytoma in pregnancy. CHF can increase plasma and urine metanephrine levels.1

Management

The patient is managed by the family physician in tandem with constant obstetrical monitoring and a prompt endocrinologist referral. While referral to a surgeon for excision of tumour is the definitive cure, clinically it is still controversial as to when it can be safely used1. Experts do agree however that diagnosis in later pregnancy is best handled with medical stabilization.
Alpha blockade should always be established before before $\beta$. If $\beta$-adrenergic blockade is attempted first to reduce blood pressure by reducing heart rate and contractility, it will also result in the loss of vasodilation caused by $\beta_2$ receptors. There will be an increased alpha effect that is unopposed by $\beta_2$, and will thus have further increased the blood pressure. The alpha blocker of choice is phenoxy-benzamine.\(^3\)

**Conclusion**

A pheochromocytoma is a rare yet hazardous form of endocrine hypertension during pregnancy which a physician should be vigilant for in patients with poorly controlled hypertension and a constellation of signs and symptoms which point to an adrenergic hormonal milieu. Medical stabilization, prompt referral and consideration of surgery are the components of proper management.

**References**

**PART I**

**PART II**