

## Osseous Metastase of Occult Paraganglioma: A Diagnostic Medical Error

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ARTICLE INFO	ABSTRACT
<p><i>Article type:</i> Case Report</p>	<p><b>Introduction:</b> Diagnostic errors have a natural complexity. Medical diagnoses make up a large proportion of all medical errors and cause much suffering and harm. Compared to other types of error, diagnostic errors receive little attention-a major factor in continuity of unacceptable rates of diagnostic error.</p> <p><b>Case:</b> A 55-year-old woman presented to the emergency department (ED) complaining of bone pain which has been started a month ago and increased gradually in the upper right thigh. Following the emergency evaluation she was sent home with pain medication. On the second visit, a femur neck fracture was seen in the x-ray. She underwent hemiarthroplasty and was discharged. Over several weeks she was reevaluated by many Physicians, because of her worsening pain. In the third visit after the surgery, her x-ray showed bone destruction and following bone biopsy, malignant paraganglioma was diagnosed.</p> <p><b>Discussion and solution:</b> In all cases in which patient comes to us with skeletal pain, getting a comprehensive history and a full physical examination are prior to lab tests and x-rays. Bone metastasis which can develop severe pain and pathological fractures, is common in patients with malignant paraganglioma.</p> <p>Effective steps for diagnostic error prevention are: Considering the diagnostic error in the normal range of quality assurance surveillance and review, identifying the elements leading to diagnostic errors and getting feedback on the diagnoses Physicians make, in order to improve their skills.</p> <p><b>Conclusion:</b> It is an every health system priority to identify, analyze, and prevent diagnostic errors in order to improve patient safety.</p>
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### Introduction

Diagnostic errors have drawn recent attention as a patient safety and public health priority (1). Unlike therapeutic errors, the measurement of diagnostic errors is difficult (2). Because of the relatively long deferment between error

occurrence and its detection, weakness in clinical documentation of important diagnostic details and the diagnostic reasoning processes (compared to medication errors), lack of consensus on the best diagnostic plan, retrospective assessments of "diagnose ability" or "preventability" of harm have become subject

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of substantial risks of perception and outcome biases(3). Nevertheless, it is commonly accepted that diagnostic errors are recognized (4), reported (5), and appreciated less than that they deserve it (6).

Diagnostic errors, especially those that are physician negligence consequence, in approximately 50% of cases lead to serious disability or death (7). Misdiagnoses are estimated to be responsible for approximately 40000-80000 preventable in-hospital deaths every year in the US by missing opportunities to apply prompt, correct treatment or by the application of incorrect treatments(1).

Bone pain is usually the first symptom of tumor which has metastasized to the bone. At the beginning, the pain may fluctuate (It comes and goes). It tends to get worse at night and get better by movement. After a while, it can become constant and may feel worse during activity. Without treatment, the bone might get so weak that it might break. If the bone metastasis is found soon enough, fractures won't happen (8).

Parangliomas (also known as extra-adrenal pheochromocytoma) are tumors that come from the sympathetic and parasympathetic nervous system. Benign or Malignant nature of these tumors has been difficult to determine by their pathological characteristics. The only way of recognizing malignancy is finding a metastatic lesion or direct invasion in a site with no residual embryonic paraganglionic tissue (9).

To our knowledge, this is one of the rare reported cases of femoral pathological fracture representing metastatic paraganglioma. This indicates that metastasis to bone with a consequent pathological fracture, may be the first manifestation of paraganglioma.

### Case Presentation

A 55-year-old female patient reported to emergency department of a general teaching hospital with the complaint of pain in left thigh. Her history revealed that the pain started one month back and had gradually increased up to that time.

In first step after physical examination, patient was discharged with the prescription of oral NSAIDS .After a week the patient returned to the same center complaining of persistent pain.

In the x-rays of left hip and femur, obvious fracture and bone irregularity was seen in femur neck .The patient was prepared for undergoing hip replacement surgery .Routine lab tests were performed and all indices was reported in the normal range. During surgery the fractured femoral head was removed, and replaced with a metal implant. She was discharged on the third

day after surgery. No further therapy was indicated other than palliative care and painkillers.

After several weeks patient came back with persistent pain .X-ray was performed and patient was sent home again on pain medication .No further follow up was done. Eventually, after one month she visited another center .The new radiography of the painful area showed more extensive bone destruction and raised the possibility of metastatic disease. The Patient underwent another surgery and a biopsy was performed. Pathological examination confirmed the diagnosis of bone metastasis due to a malignant paraganglioma. Chemo and radiotherapy was started for the patient.

### Discussion

In all cases in which patient comes to us with skeletal pain, obtaining a comprehensive history and a full physical examination are prior to lab tests and x-rays. In this case, unfortunately, no one had paid attention to the patient's history. The patient did not give any history of trauma to the hip and thigh area. She only complained of a gradually increasing pain.

Bone pain is often the first symptom of cancer that has invaded the bone. At the beginning the pain often comes and goes. It tends to worse at night and may get better by movement. Later on, it can become constant and may be worse during activity. The bone might be so weakened that it will break easily. If the bone metastasis is found early enough, such consequences can be predicted and prevented (8).

Most pheochromocytomas/ paragangliomas are benign. For a long time PGL was known as the disease of 10 % (10 % metastatic, 10 % familial, 10 %recurring, 10 % extra-adrenal, 10 % occurring in children). Nowadays, by the means of improved diagnostic techniques, the rule of 10 % does not exactly describe PGL. Overall, in 36 % of PGL patients' disease goes towards malignancy, which highly depends on the type of tumor .Most of PGL metastases occur in adjacent and distant lymphatic nodes, bones, liver and lungs (10).

Bone metastases (BM) can develop severe pain, spinal cord compression, pathological fractures, and/or hypercalcemia. These skeletal-related events (SREs) may lead to immobility, dependency to others, lower quality of life, and reduced survival. There is no enough evidence on the clinical impacts of BM and SREs in patients with malignant sympathetic paraganglioma (sPGL).

BM and SREs are common in patients with malignant sPGL. SREs often occur in a short time

after the diagnosis of BM; severe pain is the most frequent symptom. A long term follow up for on time medical or surgical intervention by a multidisciplinary team seems necessary for these patients (11).

Paraganglioma can be distinguished based on its biochemical characteristics in secreting (adrenergic, noradrenergic, or mixed) and non-secreting (biochemically silent) tumors. The origin of second type is commonly the head and neck parasympathetic tissue (10).

Although some paragangliomas, do not develop with symptoms of catecholamine secretion, (such as our patient) intratumoral transforming of catecholamines to metanephrines (norepinephrine to normetanephrine, and epinephrine to metanephrine) occurs independently of catecholamine secretion. As a result, biochemical testing is indicated in every patient with a paraganglioma even if there is no clinical manifestation of catecholamine hypersecretion (12).

PGL cells seem to spread in the body, through the both lymphatic and hematogenic route. It is difficult to determine the survival of malignant cases, because they are not usually reported in large, controlled, randomized studies (due to their rarity). Nevertheless, the survival of malignant paraganglioma is thought to be related to the familial condition, the stage of the disease at the diagnosis time, the therapeutic method, and the follow-up after surgery (13). Patients with long bone metastases have a much better prognosis with the survival of 20 years after metastases detection, while the survival of patients with soft tissue metastases is not so promising (10). Knowledge of the biochemical phenotype is an important diagnostic indicator for tumor localization and possible underlying mutation as well as the presence of metastases. At the moment, the gold standard for PGL diagnosis is an elevated plasma and/or urine metanephrine level. When a PGL is present, catecholamine levels can also be elevated in both plasma and urine, but because of their lower stability, they show a lower sensitivity as a diagnostic criterion in comparison to metanephrines (10).

### Solution

A well-judged management of such cases requires consideration of two issues. The First is importance of history elicitation and the second is paying attention to patient's history. In this case, considering absence of trauma history and other risk factors, biopsy should have been done after surgery. This mistake led to 2 month

postponement in patient's diagnosis and treatment which resulted in her early death.

In some cases of diagnostic errors, the clinician decides on a single diagnosis and fails to fully consider other diagnostic possibilities which are called "premature closure". In this case if the physician had asked a simple question "What else could this be?" the outcome of the patient might have changed significantly.

Another solution includes designing certain mechanisms to receive systematic feedback on one's diagnostic decisions, such as receiving notice when a patient discharged from the hospital or is readmitted with a different diagnosis. Although such solutions may be effective, they cannot be easily implemented.

For cases which the correct diagnosis, are absolutely dependent on the clinician's skill, using systemic interventions to aid the clinician, such as second readings of key diagnostic tests and providing backup recourses for clinical decision making ,seems beneficial . Physicians need to improve their clinical experience and skills by getting feedback on the diagnoses they make. Finally, clinicians need to identify and restrict some innate cognitive tendencies like overconfidence in order to feel the need of reasoning and everlasting learning (6).

### Conclusion

Misdiagnosis is most often linked to bedside negligence in history taking, physical examination, test ordering, or test result interpretation.

Before closing on a diagnosis, if something in your case does not seem compatible with your diagnosis, take a moment and consider using "not yet diagnosed "(14).

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