Osseous Metastase of Occult Paraganglioma: A Diagnostic Medical Error

Ghasemi TA1, Heydarian F2* Soltanifar A3

1 Forensic Medicine and Toxicology Specialist, Addiction Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
2 Associate Professor Pediatrician, Research Center for Patient Safety, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
3 Research Center for Patient Safety, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

**Article Info**

**Article type:** Case Report

**Article history:**
- Received: 24-Jul-2013
- Accepted: 3-Sep-2013

**Keywords:**
- Bone Metastase
- Diagnostic Error
- Malignant Paraganglioma
- Medical Error
- Pathologic Fracture

**Abstract**

**Introduction:** 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 continuous unacceptable rates of diagnostic error.

**Case:** 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.

**Discussion and solution:** 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.

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.

**Conclusion:** It is an every health system priority to identify, analyze, and prevent diagnostic errors in order to improve patient safety.

Please cite this paper as:


**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 became subject...
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).

Paragangliomas (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 parangangioma. 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 hypercalcaemia. 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 parangangioma (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 mul
tidisciplinary team seems necessary for these
patients (11).

Paraganglioma can be distinguished based on its biochemical characteristics in secreting (adren
ergic, noradrenergic, or mixed) and non-
secreting (biochemically silent) tumors. The ori
gin 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
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).

References

1. Newman-Toker DE, Pronovost PJ. Diagnostic
2. Newman-Toker DE, Makary MA. Measuring
Diagnostic Errors In Primary Care: The First
Step On A Path Forward. Comment On "Types
And Origins Of Diagnostic Errors In Primary
Care Settings". JAMA Intern Med. 2013;
3. Wears RL, Nemeth CP. Replacing Hindsight
With Insight: Toward Better Understanding Of