Review article

# A practical approach to secondary osteoporosis — Case studies in Asia

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## Abstract

Osteoporosis is a major health disease that is increasing in Asia especially given the rapidly aging population in many of the countries. A major aim of the management of osteoporosis is to prevent the next fracture from happening and its attendant morbidity and possible mortality. A failure to identify a possible secondary cause of osteoporosis might lead to suboptimal benefits of treatment or possibly treatment failure. This article aims to use a series of cases in order to best illustrate the approach to the screening of secondary causes of osteoporosis and highlight learning points from each case with a slant towards the management of patients in Asia, focusing on the East and South East Asia (SEA).
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*Keywords:* Osteoporosis; Asia

## 1. Introduction

Osteoporosis is a major health disease that is increasing especially given the rapidly aging population in many parts of the world. An integral goal of the management of osteoporosis is to prevent the next fracture from happening and its attendant morbidity and possible mortality. A failure to identify a possible secondary cause of osteoporosis might lead to sub-optimal benefits of treatment or possibly treatment failure, not to mention the non-bone consequences of the condition.

There are unfortunately many causes of secondary osteoporosis. When we should screen for them and how extensive the workup should be is still a matter of debate. To date there is a paucity of cost-analysis studies with regards to the screening of secondary causes or even which tests should be included in the initial assessment, especially in Asia. Various studies include different cohorts of patients and different selection of investigations. Clinicians have to decide then when to embark on a search for these causes and which tests to use for initial screening.

This article aims to use a series of cases in order to best illustrate the approach to the screening of secondary causes of osteoporosis and highlight learning points from each case with a slant towards the management of patients in Asia, focusing on the East and South East Asia (SEA).

### 1.1. Case 1

A 65-year-old woman is referred to an endocrine clinic for management of her osteoporosis. She had bent down to pick up a cup that she had dropped and felt a sudden pain in her back. An x-ray showed that she had sustained a T12 compression fracture. Her bone mineral density (BMD) is as shown:

| | Spine (L1-L4) | Total hip (TH) | Neck of femur (NOF) |
|---|---|---|---|
| T-score | −1.3 | −2.6 | −2.7 |

The questions to ask for this patient in order to appropriately treat her are these:

1) Does the patient have osteoporosis?

The answer is yes both clinically and by bone mineral density criteria as set out by the WHO. She had suffered a

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fragility or low trauma fracture from less than a standing height. This means a fracture from a force that does not justify a fracture. This satisfies the clinical definition of osteoporosis − a condition where the bones are brittle and susceptible to fracture. By BMD criteria osteoporosis can also be diagnosed via a T-score $\leq -2.5$ in any of the 3 regions of interest (ROI) as denoted above.

Note that the spine for this patient showed a relatively dense BMD as compared to the other regions. This might be due to osteosclerosis and/or osteophytes present in an elderly patient, inaccurately increasing the BMD in that region. Indeed, it was found that about 46% of females between the ages of 40−84 years of age had osteophytes and this increased with increasing age [1].

2) Now that you have ascertained that the patient indeed has osteoporosis, do you screen for secondary causes of osteoporosis and if so, which ones?

To answer this question, several factors should be taken note of:

- The list of possible secondary causes of osteoporosis are many and shown in Table 1.
- It is estimated that there are about 200 million patients worldwide with osteoporosis and this number is estimated to increase [2].
- Globally and in Asia, the elderly population is rapidly increasing. Indeed, in Singapore, the proportion of the population aged 65 years and above was 7.3% in 2000 and this is projected to increase to 18.7% in 2030 [3].
- About 30% of patients with postmenopausal osteoporosis will have secondary causes of osteoporosis [4].

Taking into account the figures above and hence the sheer volume of cases, it would certainly not be cost-effective to screen for all secondary causes of osteoporosis for all postmenopausal patients. Yung et al. showed that in the patients referred to an osteoporosis clinic in a tertiary hospital in Singapore, secondary causes included the following- Vitamin D deficiency in 18.5%, hyperthyroidism in 10.1%, primary hyperparathyroidism in 1%, secondary hyperparathyroidism in 6%, hypercalciuria in 21.6% and glucocorticoid use in 8.4% of the patients. The mean calcium intake was 660 mg per day [5]. Bour et al. reported that about a quarter of patients presenting with an osteoporotic fracture to an emergency department in the Netherlands had a known secondary cause of osteoporosis on presentation and a quarter of the patients had a newly discovered secondary cause after investigations. More than 90% of the study participants were found to have an inadequate calcium (recognized as 1200 mg in the study) and about two thirds had vitamin D deficiency (recognized as < 50 nmol/L in the study) [6].

A universally agreed upon list of screening tests to be carried out in the pursuit of secondary causes of osteoporosis has not been settled on and varies with differing studies and practices. Table 2 gives some of the more common tests that are routinely performed. The first segment would be more commonly performed as opposed to the second. In an ideal situation, it might be prudent to screen all patients and to screen for the commonest causes. A thorough history and physical examination might contain clues to help pinpoint a secondary cause and focus the investigations. The list of possible causes in Table 1 would be helpful in tailoring the questions and also physical examination.

However, the approach depends on the individual circumstances of the patients. For instance, if the patient in case 1 was in a primary medical facility with no resources other than a bisphosphonate at hand and no financial ability or technical capability of further managing the secondary cause, screening for secondary causes of osteoporosis becomes a moot point. Even should a secondary cause exist and there was a further drop in the bone mineral density upon follow-up consultation,

Table 1
Secondary causes of osteoporosis.

- Endocrine disorders such as hyperthyroidism, hyperparathyroidism, Cushing's syndrome whether exogenous or endogenous, hypogonadism, acromegaly, diabetes mellitus, idiopathic hyperacalciuria, early menopause.
- Gastrointestinal diseases − inflammatory bowel disease, severe liver diseases, malsorption syndromes
- Hematologic diseases eg multiple myeloma, mastocytosis
- Rheumatological diseases eg rheumatoid arthritis
- Drug induced osteoporosis
    − Steroids, anti-epileptic drugs, anti-depressants, glitazones, proton pump inhibitors (PPIs), thyroxine, aromatase inhibitors, GnRH agonists
- Genetic disorders such as osteogenesis imperfect, hypophosphatasia
- Others: Immobilization, smoking, low BMI, HIV infection, heavy alcohol use, organ transplantation, poor accrual of bone health from deprivation in early years from either systemic illnesses

Table 2
Investigations for secondary osteoporosis.

More routinely done:
- Full blood count
    - The hemoglobin levels are of especial interest as both a marker of chronic disease and also the triad of anemia, hypercalcemia and increased creatinine may signify multiple myeloma
- Urea, electrolytes and creatinine − in order not to miss renal bone disease
- Thyroid function screen
- 25-OH Vitamin D
- Ca with or without PTH
- Testosterone − for males
- 24 hours urine calcium
- Liver function test

Other tests to consider:
- Screening for endogenous Cushing's syndrome when suspected − such as the overnight dexamethasone suppression test or the 24 hours urine free cortisol
- Screening for coeliac's disease - this is a rare condition in East and South East Asia and as such rarely is a first line test to be carried out.
- Protein electrophoresis for multiple myeloma − given that this is relatively rare and also relatively more expensive to carry out requiring specialised laboratories, it is generally not first line of choice for investigations.

PTH, parathyroid hormone.