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NOTE

A Potential Risk for Osteomalacia due to Sociocultural Lyfestyle in Turkish Women

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Abstract. Osteomalacia is a metabolic bone disease caused by deficiency of vitamin D or its active metabolites. Because poor sunlight exposure is one of the most common causes of osteomalacia, the disease seems to be rare in countries with adequate sunlight We report nine Turkish female patients with osteomalacia with ages between 21 and 50 years. Osteomalacia was diagnosed on the basis of a history of bone aches or pains, muscle weakness, low or low normal serum calcium and urinary calcium, decreased concentrations of serum inorganic phosphorus and 25- hydroxyvitamin D and increased serum intact PTH and alkaline phosphatase levels. Radiographically, pseudo-fractures were present in seven of the patients. The patients' symptoms and signs were relieved with the treatment with vitamin D analogues and calcium. Their hypovitaminosis D are suggested to be caused by excessive clothing in the outdoors due to sociocultural and religious reasons. Excessive clothing may be a risk factor for osteomalacia in young to middle-aged and otherwise healthy women even in countries with adequate sunlight.

Key words: Osteomalacia, Vitamin D deficiency

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OSTEOMALACIA is a metabolic bone disease caused mainly by deficiency of vitamin D or its active metabolites. Bone pain, muscle weakness and difficulty in walking are the characteristic clinical features of the osteomalacia syndrome. Low vitamin D intake and poor exposure to sunlight are the most common causes of vitamin D deficiency. This is especially true of elderly patients who are hospitalized, institutionalized or stay indoors and fail to receive either adequate sunlight exposure or dietary supplements of vitamin D [1–3]. Covering skin in the outdoors was suggested to be a contributing factor to the development of osteomalacia particularly in strict vegetarians, but it had not been reported as a predisposing major factor in otherwise healthy women, especially those who have been living in countries with adequate sunlight [4–9].

Osteomalacia in adults may go unrecognized even in the presence of classical symptoms [10]. The disease is frequently omitted in diagnostic considerations and a delay in treatment is notable in many of the patients.

We here by report symptomatic hypovitaminosis D in nine women who habitually covered their skin in the outdoors. The time between the beginning of the symptoms, the initial recourse to a doctor and establishment of the correct diagnosis of osteomalacia is also stressed.

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Patients, Methods and Results

Osteomalacia was diagnosed on the basis of a history bone aches and pains, muscle weakness,

low serum and urinary calcium, low concentrations of serum 25-hydroxyvitamin D and increased serum PTH levels. We analyzed the hospital notes and past medical histories of the patients.

Table 1 shows the clinical data of the patients. The ages were between 21 and 50 years and all were menstruating regularly. Duration of the complaints before diagnosis varied from 4 to 120 months. Laboratory results for the patients at referral are given in Table 2. All of them had low or low normal plasma total and ionized calcium and phosphate concentrations, high alkaline phosphatase, low urinary calcium, low serum 25-hydroxyvitamin D and increased serum PTH concentrations. Osteopenia was present in all the patients radiologically and pseudofractures (Looser's zones) were observed in seven of them.

None of the patients had any clinical or biochemical evidence of renal, gastrointestinal, hepatic or malignant diseases. They also had no drug histories. They were all on normal diets, and none of them were vegetarians. Interestingly, they all were covering their skin when outdoors, for sociocultural and religious reasons, and this was the main pathogenetic mechanism in the development of hypovitaminosis D osteopathy.

In retrospective analysis the symptoms of the patients were typical for osteomalacia from the beginning but remained unrecognized or misinterpreted. Previous referrals were orthopedic surgeons, neurologists or rheumatologists. All patients were prescribed non-steroidal antiinflammatory drugs. In two of the cases misinterpretations had serious therapeutic consequences. Cases 1 and 7 were diagnosed to have osteoporosis and were treated with salmon calcitonin and developed clinical carpopedal spasms. Cases 2 and 4 were referred for orthopedic

Table 1. Clinical data of the patients with hypovitaminosis D

Case	Age (years)	Parity	Duration of complaints until referral (months)	Complaints	Other referrals	Treatment before diagnosis
1	27	2	12	Pain in back, shoulders, hips,	Rheumatologist	NSAID, Etidronate, Calcium, Calcitonin Salazopyrin
2	21	–	48	Pain in neck, legs, back, muscle weakness, difficulty in walking	Orthopedic surgery	NSAID,
3	37	8	48	Pain in back, legs, muscles, difficulty in walking, muscle weakness	–	NSAID
4	29	–	120	Difficulty in walking, pain in legs, muscles, muscle weakness	Orthopedic surgery, Neurology	Surgical operation, NSAID
5	40	2	12	Pain in back, shoulders, legs, muscle weakness, difficulty in walking	Rheumatologist	NSAID
6	43	2	12	Pain in muscles, back, difficulty in walking	–	NSAID
7	50	5	4	Muscle spasms, paresthesias	Rheumatologist, Neurology	Calcitonin calcium
8	29	2	24	Pain in back, muscle weakness, difficulty in walking, paresthesias	Rheumatologist, Neurology	NSAID
9	29	2	36	Pain in shoulders, knees, difficulty in walking, paresthesias	Rheumatologist	NSAID

NSAID, nonsteroid antiinflammatory drugs.

Table 2. Laboratory results for the patients at the time of diagnosis of the osteomalacia

Case No	Total calcium (mmol/L)	Ionized calcium (mmol/L)	Phosphate (mmol/L)	Alkaline phosphatase (IU/L)	Urinary calcium (mmol/d)	PTH intact (ng/L)	25-OH vitamin D (nmol/L)
1	2.0	0.95	0.74	235	0.61	384	14
2	1.9	0.83	0.68	315	0.49	178	10
3	1.8	0.94	0.42	567	0.38	342	6
4	2.15	0.99	0.45	198	0.55	148	15
5	2.15	0.87	0.68	218	0.88	124	8
6	2.1	0.96	0.61	348	0.28	528	2
7	2.0	0.82	0.68	376	0.73	987	16
8	2.15	1.1	0.68	194	0.89	219	10
9	1.5	0.82	0.81	158	0.92	604	9
Normal range	2.15–2.5	1.1–1.32	0.91–1.45	35–134	1.25–7.5	12–72	25–100

surgery because of their pseudofractures in both femoral shafts and case 4 was also operated on with a diagnosis of true fracture. The symptoms and signs of case 8 were assessed as psychological by the first consulting doctor.

For 25(OH) D measurements a ^{125}I RIA kit (Incstar, Minnesota, USA) was used. This assay consisted of a two-step procedure. After a rapid extraction of 25(OH) D from serum with acetonitrile, the treated sample was then assayed by an equilibrium RIA procedure. The coefficient of variance of the assay was less than 10%.

All patients were given either vitamin D (400 IU/day) or 1,25 OH D3 (0.5–1 μg/day) and calcium. They all become free of symptoms and biochemical and radiological abnormalities became normal with the treatment. Drugs were discontinued after six months and all were educated about the importance of adequate exposure to sunlight. Seven of the patients remained symptom free without any medication. In two of them, who refused to change their life styles, symptoms of hypovitaminosis D reappeared and Vitamin D supplementation was restarted and they did well with the treatment.

Discussion

Osteomalacia is the failure of the organic matrix of bone to mineralize normally. The most frequent underlying biochemical cause of mineralization defect is a decrease in the calcium and/or phosphate concentrations in the extracellular fluid. Vitamin D deficiency is the major cause of the disease. Whereas it was formerly thought that vitamin D deficiency due to inadequate sunlight exposure rarely caused osteomalacia, certain social, environmental and cultural developments have almost certainly led to an increased incidence of this problem [4–8]. Usually this problem was suggested to be confined to the elderly [1–3], but it was also reported that migrating from areas of intense ultraviolet exposure to areas with marginal ultraviolet exposure can lead to the development of osteomalacia, especially in people who habitually cover their skin excessively. This phenomenon has been reported mostly from Great Britain among immigrants from India and Pakistan [4–9].

Vitamin D is derived from skin and oral intake but the skin generation by direct action of the UV rays contained in sunlight is the main source of Vitamin D in humans. In the case of limited UV light exposure, dietary factors determine the development of osteomalacia. Strict vegetarianism and female sex were reported to increase the risk [4, 7, 8]. Although low oral vitamin D intake had been detected in some European countries [10] increased prevalence of osteomalacia among young women was not reported. Oral intake could also be low in our patients since the natural dietary sources of vitamin D are limited, but inadequate exposure to sunlight as a result of excessively covering their skin when outdoors for traditional and religious reasons had to be the major determinant of osteomalacia development since dietary factors gain importance only in the case of

limited UV light exposure.

The biochemical results for our patients— increased alkaline phosphatase and PTH, low- low normal total and ionized calcium, phosphate and 25OH D levels— are typical of osteomalacia due to vitamin D deficiency. Looser's transformation zones (pseudofractures), which are pathognomonic for osteomalacia, was observed in seven (78%) of the nine patients.

Another problem was the delay in diagnosing osteomalacia in our patients. Nellen *et al.* [11] also observed such a delay in their patients and they attributed it to unfamiliarity with the clinical picture of hypovitaminosis D. Since the bone pain is usually dull, poorly localized and felt in the bones, it can be unrecognized and can cause the physician to misdiagnose, as in our cases. Although the laboratory data of the present patients were all characteristics of osteomalacia, establishing the correct diagnosis had taken a very long time. Questioning the patients with special attention to sunlight exposure is crucial. Peach *et al.* [9] found that questions on such factors as covering up arms and legs when going outdoors was valuable in defining osteomalacic patients.

In conclusion, the lack of exposure to sunlight has a significant effect on the vitamin D status, especially in women who wear excessive clothing in the outdoors, since endogenous cutaneous synthesis of vitamin D is very important. Limited UV light can lead to hypovitaminosis D osteopathy in healthy women with no other risk factors. Since there are a lot of women who excessively cover their skin in the outdoors in our country and in some other countries in the world there may be a great number in the female population who are at risk for osteomalacia. The disorder may remain undiagnosed for a long time, and in order to prevent this undesirable delay and unnecessary studies, the phenomenon "osteomalacia due to poor solar exposure" should be kept in mind in such patients.

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