

Vitamin D deficiency: an unrecognized cause of flank pain

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Abstract Loin pain is frequently not associated with any urinary abnormality. Musculoskeletal abnormalities are not uncommon as alternative cause of flank pain. Osteomalacia of the ribs was infrequently encountered as the cause of flank pain. Vitamin D deficiency has been reported as a common problem worldwide with special predilection to the Middle East area. In this study, we looked for vitamin D deficiency in patients with flank pain associated with tenderness over the tips of the lowermost ribs. Out of 783 patients presenting with unilateral or bilateral flank pain to a single center over a period of 3 years, 316 did not have a definite urologic cause (group B). One hundred and eighty-seven of these patients had distinct tenderness over the costal margin (group B1) that could not be explained by history and radiology. All patients of group B were tested for serum levels of 25(OH) vitamin D. Very low serum levels of 25(OH) vitamin D was detected in all cases of group B1 and in only in only 26.4% of the remaining cases of group B (group B2). Relief of flank pain was noticed within 2 months in 55.1% of vitamin D deficient cases. In patients presenting with flank pain, the existence of tenderness of the last ribs instead of the renal angle proper should alert to a possible cause in the rib cage. Estimation of serum vitamin D level should be performed in these cases.

Keywords Loin pain · Flank pain · Nephrolithiasis · Osteomalacia · Vitamin D deficiency

Introduction

Flank pain is an important symptom of different urologic diseases. In addition to urologic causes, gastrointestinal, musculoskeletal, pleural, and neurologic diseases might be the source of this pain instead. The pain related to the last three ribs usually mimics renal pain. Because the definite cause of pain related to these ribs was not recognized in most cases, the term “12th rib syndrome” was suggested. Unfortunately, this syndrome is frequently overlooked, especially after the routine use of spiral non-contrast computerized tomography (SCT) to investigate patients presenting with flank pain and neglect of thorough clinical examination. Clinical examination to elicit tenderness over the tip of the lowermost ribs is necessary to raise this possibility [1]. The “hooking maneuver”, first described in 1977, is a good alternative test [2]. The examining clinician can do this test by insinuating the hand underneath the costal margin and pulling anteriorly. This maneuver can elicit pain of variable severity. The 12th rib syndrome was first described in 1919 as a cause of flank pain [3]. Consequently, further newer reports have further characterized the condition [4–6]. These newer reports were mostly anecdotal or descriptive case series. However, two investigators reported this syndrome in 1–5% of patients attending internal medicine or gastroenterology clinics [7, 8]. The underlying pathology of the 12th rib syndrome was not defined. Osteomalacia of the ribs as the cause of flank pain in a Vietnamese patient was disclosed by a recent case report [9]. The long-term use of tenofovir was behind osteomalacia in this case. Six years earlier, Sievenpiper et al. have described a 53 year old

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Pakistani woman with history of mastectomy of the right breast for invasive ductal carcinoma 2 years earlier. This lady presented on follow-up with musculoskeletal pains at different sites including the right loin. She was initially managed with multiple courses of chemotherapy that failed to control her symptoms. Later on, she was accidentally discovered to have severe vitamin D deficiency [10].

Materials and methods

This study spent 3 years starting by January 2014 to evaluate 783 consecutive patients that presented with distressing unilateral or bilateral flank pain to the international kidney center, Nasr City, Cairo, Egypt. After routine history taking and clinical examination, these patients underwent routine laboratory, and imaging work-up including abdomino-pelvic ultrasonography and spiral non-contrast computerized tomography (SCT) of the urinary tract. Four hundred and sixty-seven cases proved to have a urology cause for their presenting pain (group A). These causes included stones, pelvi-ureteric junction and ureteric obstruction, urinary tract infection, and renal cysts or neoplasms. Among the patients with negative urinalysis and imaging studies (316 cases, group B), 187 cases have shown appreciable tenderness elicited on palpating the lowermost ribs at the costal margin on either side of the thoracic cage with maximum tenderness over the tips of the involved ribs (group B1). A single examiner did clinical examination of all patients before performing different laboratory investigations. The routine laboratory and imaging studies of these patients excluded the urinary tract as the cause of flank pain in these cases. The possibility of osteomalacia was raised. Accordingly, serum level of calcium, phosphorus, alkaline phosphatase, 25(OH) vitamin D, and parathyroid hormone (PTH) were tested for all patients of group B1 and group B2.

Microsoft computer statistics package was used for data analysis. Data were summarized as mean and standard deviation. Comparison between groups was evaluated using Student's *t* test.

Results

Results are summarized in Tables 1 and 2. The serum level of 25(OH) vitamin D disclosed moderate to severe vitamin D deficiency in subjects of group B1. In addition, serum alkaline phosphatase and serum PTH were significantly higher in this group. In order to avoid the confounding effect of impaired kidney function on the studied parameters, further analysis was performed after exclusion of chronic kidney disease patients. Thirty-one and 23 cases were excluded in group B1 and group B2, respectively. The significant difference in serum levels of 25(OH) vitamin D, PTH, and alkaline phosphatase between the two groups was still observed (Table 2). When vitamin D deficient patient were prescribed vitamin D replacement, 55.1% (103 patients) of group B1 reported dramatic relief of flank pain within 2 months after onset of replacement.

Discussion

The first report of osteomalacia as the cause of flank pain was in 2008. In this report, Sevenpiper et al. described a 53 years old Pakistani woman that was erroneously treated by chemotherapy when presented with pain in multiple sites including her right loin after radical mastectomy for breast cancer. This lady later proved to have severe vitamin D deficiency after she developed manifestations of hypocalcemia [10]. Six years later, Hamnvik et al., described a Vietnamese patient with flank pain. The underlying mechanism of osteomalacia in this case was a consequence of

Table 1 Demographic data and laboratory investigations

Parameter	Group B1		Group B2		P value
	Range	Mean \pm SD	Range	Mean \pm SD	
Age (years)	19–65	38 \pm 8.75	26–43	37 \pm 4.87	< 0.01
Gender (M/F)	11/176		14/115		
BMI (kg/m ²)	19.5–36	29.5 \pm 2.71	17.5–31	24 \pm 2.99	< 0.001
BUN (mg/dL)	8–35	11 \pm 3.91	12–25	10.9 \pm 3.34	NS
Serum creatinine (mg/dL)	0.6–2.3	0.9 \pm 0.57	0.6–2.0	0.93 \pm 0.49	NS
Serum calcium (mg/dL)	7.9–9.2	8.5 \pm 0.28	8.1–9.1	8.4 \pm 0.3	NS
Serum phosphorus (mg/dL)	3.0–4.8	4.1 \pm 0.64	3.4–5.5	4 \pm 0.67	NS
Serum alkaline phosphatase (U/L)	55–186	128 \pm 38	44–140	119 \pm 27	< 0.01
Serum PTH (pg/mL)	44.3–198.5	87.8 \pm 14.04	44–51.4	47.9 \pm 2.52	< 0.001
Serum 25(OH) vitamin D (ng/mL)	4.8–21	12.8 \pm 5.8	21.8–49.8	37 \pm 8.43	< 0.001
Serum uric acid (mg/dL)	3.7–7.9	4.9 \pm 1.13	4–5.9	4.9 \pm 0.48	NS

Table 2 Demographic data and laboratory investigations after exclusion of CKD patients

Parameter	Group B1		Group B2		P value
	Range	Mean \pm SD	Range	Mean \pm SD	
Age (years)	19–59	34 \pm 6.5	27–41	34.4 \pm 4.06	NS
Gender (M/F)	9/147		13/93		
BMI (kg/m ²)	21–36	29.1 \pm 2.2	22.5–31	25.6 \pm 2.09	< 0.001
BUN (mg/dL)	8–17	10 \pm 2.11	12–18	10.2 \pm 1.85	NS
Serum creatinine (mg/dL)	0.6–1.1	0.8 \pm 0.1	0.6–1.0	0.8 \pm 0.09	NS
Serum calcium (mg/dL)	8.1–9.2	8.6 \pm 0.25	8.1–9.0	8.5 \pm 0.27	NS
Serum phosphorus (mg/dL)	3.0–4.2	3.5 \pm 0.55	3.4–4.3	3.6 \pm 0.47	NS
Serum alkaline phosphatase (U/L)	55–181	127 \pm 37	44–118	95 \pm 19	< 0.001
Serum PTH (pg/mL)	49–198.5	91.5 \pm 13.4	44–48.6	45.6 \pm 1.34	< 0.001
Serum 25(OH) vitamin D (ng/mL)	8–21	14.4 \pm 5	22.5–49.8	37.3 \pm 7.6	< 0.001
Serum uric acid (mg/dL)	3.7–6.4	4.2 \pm 0.78	4–5.1	4.2 \pm 0.48	NS

the long-term use of tenofovir to treat chronic hepatitis B. However, vitamin D deficiency as a cause of localized unilateral or bilateral loin pain is not reported when the literature is searched. To our knowledge, this study is the first to disclose vitamin D deficiency as a cause of flank pain. Eighty-five percent of patients in the present study are Egyptians. However, other nationalities of the adjacent Arab countries (Libya, Syria, Saudi Arabia, Yemen, Sudan, and Somali) were presented in the current study and constitute 15% of the cases. The prevalence of vitamin D deficiency in these countries is high in spite of the sunny weather most days. Lack of sun exposure is mostly related to social and religious habits. The poor nutrition in some countries is an additional factor.

In spite of the significant deficiency of vitamin D in these cases, the level of serum calcium and phosphorus failed to help in diagnosis. The significant increase of serum alkaline phosphatase and PTH in some of these cases might help in diagnosis in some cases. However, such approach is not sensitive or specific. The definitive diagnosis should be established by estimating serum 25(OH) vitamin D level. This statement should be amended to chronic kidney disease patients. The presence of bone pains in these cases before starting dialysis is unlikely attributed to bone mineral disorders encountered in these patients. The presence of tenderness over the rib tips instead of the renal angle must, therefore, raise the possibility of disease in the rib cage. After the exclusion of traumatic, inflammatory and neoplastic possibilities, estimation of serum 25-hydroxyl vitamin D level is advisable.

Conclusion

Part of the differential diagnosis for both acute and chronic flank pain includes the nearly forgotten condition of “12th rib syndrome”. This has also been described as a form of intercostal neuralgia and is often be overlooked by the urological surgeon, especially in an age where spiral CT has almost replaced a thorough clinical examination for patients with flank pain. A history of stone formation or indeed a confirmed urinary tract calculus should not distract the examining clinician from considering “12th rib syndrome” as a possible diagnosis. Confirmation is made by careful clinical examination, elicited by exactly reproducing the patient’s pain on point compression over the tip of the involved rib, usually the 12th or 11th or at the 10th costochondral junction. Part of the differential diagnosis for both acute and chronic flank pain includes the nearly forgotten condition of “12th rib syndrome”. This has also been described as a form of intercostal neuralgia and is often be overlooked by the urological surgeon, especially in an age where spiral CT has almost replaced a thorough clinical examination for patients with flank pain. A history of stone formation or indeed a confirmed urinary tract calculus should not distract the examining clinician from considering “12th rib syndrome” as a possible diagnosis. Confirmation is made by careful clinical examination, elicited by exactly reproducing the patient’s pain on point compression over the tip of the involved rib, usually the 12th or 11th or at the 10th costochondral junction. As the data provided here just suggest that vitamin D deficiency is one of causes of flank

pain in patients with positive signs of 12th rib syndrome, we advise to estimate the serum level of 25(OH) vitamin D in these patients.

Author contributions Professor UAASED and Professor MMS suggested the hypothesis and objectives of this study, Dr. DOA collected the necessary literature, all authors shared in collection of the study subjects, Prof. UAASED wrote the manuscript, Dr. DOA made the final revision.

Compliance with ethical standards

Funds This study did not receive funds.

Ethical committee approval This work was approved by the local ethical committee of the International Kidney Center, Nasr City, Cairo, Egypt.

Conflict of interest The authors have declared that no conflict of interest exists.

Human and animal rights All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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