Incidental finding of sacral hemiagenesis on the ^{99m}Tc-MDP bone scan as a casual regression syndrome type II

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Abstract

A 69 years old woman with chronic low back pain referred to our Department for bone scintigraphy. Patient did not have any other complaint and his physical examination of the patient was normal. Whole-body scan was acquired 3 h after the intravenous injection of 740 MBq of technetium-99m methylene diphosphonate (^{99m}Tc-MDP). Distal sacrococcygeal region could not be observed during the visual analysis of the whole-body scan. Pelvic X-rays radiography and pelvic computed tomography of the patient, demonstrated hemiagenesis of the sacrum, which was consistent with type-2 sacral agenesis. Other structural abnormalities were not detected on the pelvic CT scan of the patient. This case is presented to demonstrate the rare congenital anomaly of sacral hemiagenesis causing empty pelvis appearance in the posterior projection of ^{99m}Tc-MDP whole body bone scan. This congenital anomaly could be associated with extensive abnormalities of the lower vertebrae, pelvis, and spine.

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Introduction

Caudal regression syndrome (CRS) is characterized by abnormal development of the caudal mesoderm causing a wide range of anomalies of the hind end of the trunk. Associated mal-development of the notochord, results in various vertebral anomalies. The spectrum of these abnormalities ranges from partial absence of the sacrum causing no apparent symptoms, to extensive abnormalities of the lower vertebrae, pelvis, and spine [1-3]. Anomalies of the central nervous, musculoskeletal, genitourinary, cardiac, respiratory and gastrointestinal systems are frequently found in association with CRS. Other abnormalities reflect the degree of impairment of the embryo's mid-posterior axis mesoderm [3-5]. Since the frequency of malformations associated with CRS is very high, after diagnosing one of these malformations, a complete clinical and laboratory examination may identify other symptoms or signs of this syndrome.

Although, early vaginal ultrasound (US) can be used to detect possible lesions and inappropriate crown–rump length may be the first sign of CRS, the diagnosis of CRS is usually established in early childhood. In mildly affected patients with sacral hemiagenesis, other abnormalities may be subtle and diagnosis delayed, as in our case [6,7].

Case report

A 69 years old woman with chronic low back pain referred to our Department for bone scintigraphy. Whole-body scan was acquired 3 h after the intravenous injection of 740 MBq of technetium-99m methylene diphosphonate (^{99m}Tc-MDP). There was not any scintigaphic finding to explain the complaints of the patient but distal sacrococcygeal region could not be observed during the qualitative evaluation of the whole-body scan. (Fig. 1) Pelvic X-rays radiography and pelvic computed tomography (CT) demonstrated the hemiagenetic sacrum, which was consistent with type-2 sacral agenesis (Fig. 2) [8]. Otherwise, any structural abnormalities were not detected on the pelvic CT scan. Patient did not have any other complaint and his physical examination was normal.

This case is presented to demonstrate the incidentally discovered sacral hemiagenesis causing empty pelvis appearance on the posterior projection of ^{99m}Tc-MDP whole body bone scan.

Discussion

Bernard Duhamel (1961) first used the term "the syndrome of caudal regression" and described this syndrome as a spectrum of congenital malformations, consisting of anomalies of

Table 1. *Renshaw classification* [8]

Type	Findings
I	Partial or total unilateral sacral agenesis
II	Partial but bilateral and symmetrical sacral agenesis
III	Total sacral agenesis and variable lumbar agenesis (The iliac bones articulated laterally to the last lumbar vertebra)
IV	Complete sacral agenesis with the iliac bones fused together underneath the last lumbar vertebra

the rectum, the urinary and genital systems, the lumbosacral spine, and the lower limbs [9]. The most severe end of the spectrum is fusion of the lower limbs and major organ malformations. This is known as sirenomelia or mermaid syndrome [5]. Prognosis depends on the level of spinal defect and on the associated malformations, since some of them are, by themselves, lethal.

Sacral agenesis, a component of the CRS is a rare disorder, with a reported incidence of 0.01 to 0.05 per 1000 live births [10]. A number of classification systems exist for sacral agenesis. Renshaw S. (1978) classification (Table 1) is based on the amount of the remaining sacrum and the type of articulation between the spine and the pelvis (Fig. 3) [8, 11].

Patients with Renshaw type I or II sacral agenesis have varying degrees of motor paralysis and nearly intact sensation. Many have some lower extremity contractures, but most of them are ambulatory [12]. Patients with type III or IV sacral agenesis have a higher level of motor paralysis, more severe contractures of the lower extremities and can have spinopelvic instability. Ambulatory potential decreases as Renshaw type increases, and most of types III and IV patients cannot ambulate without significant bracing and crutches [8, 13, 14]. Since the distal half of the sacrum of the patient was not seen on scans and any other structural abnormalities were not detected on the pelvic CT scan of the patient, this hemiagenetic appearance is consistent with type-2 sacral agenesis according to Renshaw classification.

Although the process leading to the development of CRS has not been established, it has been proposed that one or more processes of primitive streak migration, primary or secondary neurulation, or differentiation are compromised before the fourth week of gestation causing a disturbance of the caudal mesoderm [3, 5, 15]. Faulty retrogressive differentiation results in disruption of the maturation of the caudal portion of the spinal cord complex, leading to varying degree of motricity deficits and of neurologic impairment.

During the neurulation period, the caudal end of the neur-

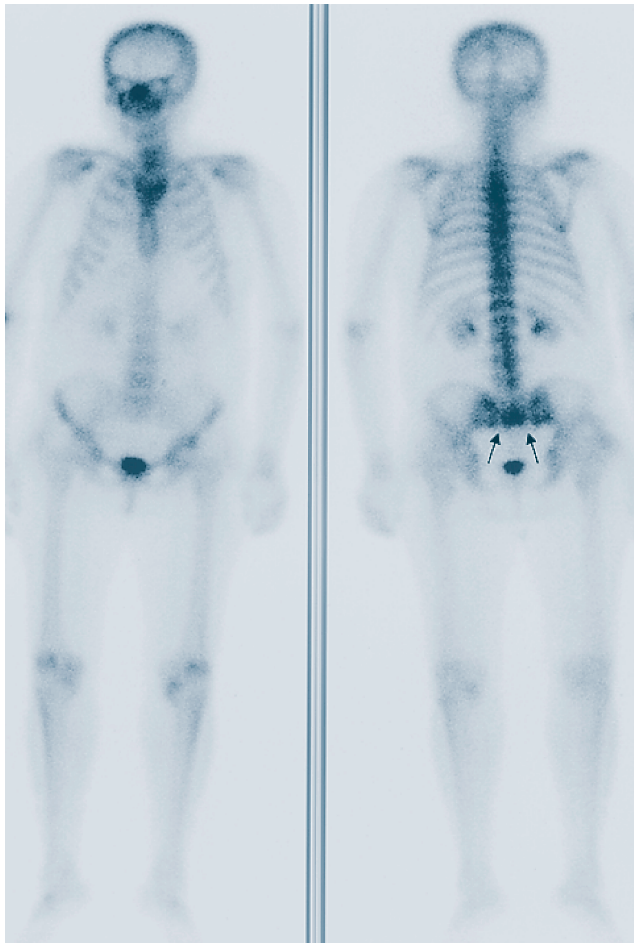

Figure 1. Distal sacrococcygeal region could not be clearly seen on the posterior projection of the whole body bone scintiscan causing empty pelvis appearance (arrows). Otherwise the scintiscan is normal.

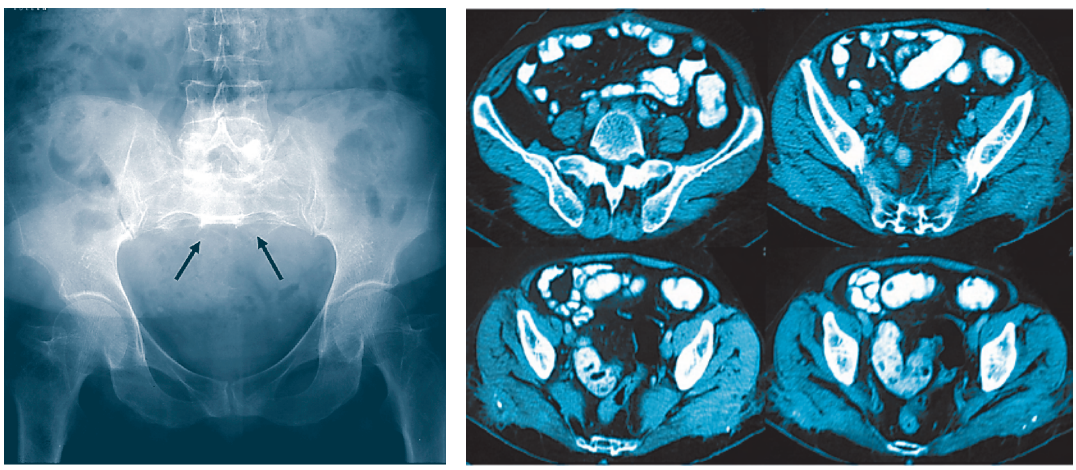

Figure 2. Frontal radiograph (A) and computed tomography slices (B) of the pelvis of the patient also demonstrate the presence of sacral hemiagenesis.

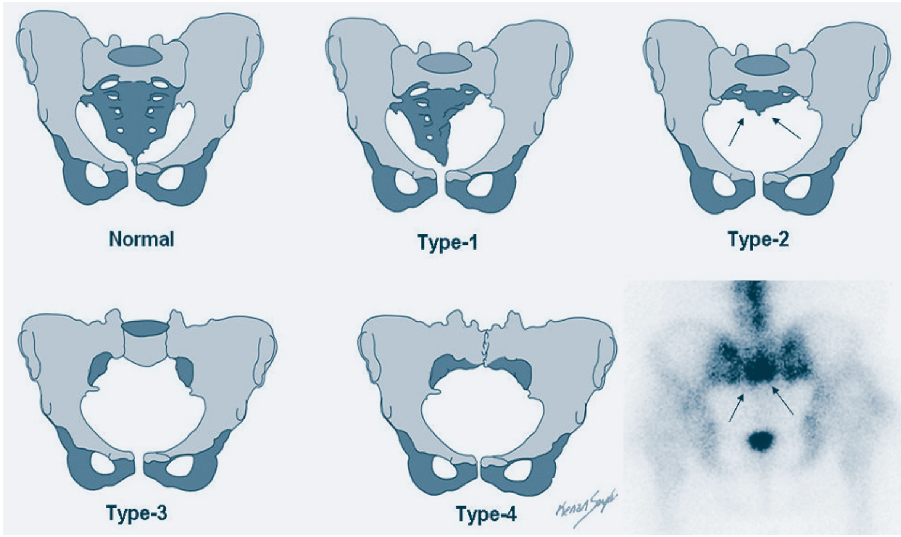

Figure 3. Schematic representation of subtypes of sacral agenesis according to Renshaw classification [7]. Scintigraphic and radiologic findings of our case are consistent with type-2 sacral hemiagenesis (arrows).

al tube and the caudal end of notochord, blend into the caudal cell mass. The caudal cell mass extends into the tail fold, adjacent to the distal end of the developing hindgut and the mesonephros. This juxtaposition of developing hindgut, genitourinary, notochordal, and neural structures within the tail fold, appears to account for the common association of distal vertebral, neural, anorectal, renal, and genital anomalies, usually observed in CRS [16, 17]. Although, US diagnosis of CRS is possible as early as at the end of the first trimester and is even more accurate with vaginal US [18]. Magnetic resonance imaging enables to evaluate the spectrum of developmental anomalies observed in patients with the caudal regression syndrome and to relate them to the pathogenesis of this syndrome [19].

The exact etiology of this syndrome is unclear, but maternal diabetes, genetic factors, teratogens and vascular anomalies altering blood flow have been hypothesized to play a role in its pathogenesis. The majority of cases of CRS are sporadic, but at least partial genetic contribution to the development of this syndrome has been reported [5, 11]. Some familial cases also suggest a genetic factor, such as autosomal dominant transmission of an abnormality on the 6th chromosome [20]. It is believed that transmission is linked to an abnormal X chromosome and affected on a dominant basis; a homozygous condition is then lethal [21].

The most commonly recognized teratogen involved in this syndrome is hyperglycemia. Women with diabetes who are dependant on insulin are 200-400 times more likely to have a child with CRS than women without diabetes, making CRS the most characteristic fetal abnormality of diabetic embryopathy [22, 23]. In animal studies, hyperglycemia has induced malformations in a dose-related fashion: a 20% malformation rate was induced at glucose levels twice normal, whereas a virtual 100% rate was induced at glucose levels of 950 mg/dl *[24].* However, history of maternal diabetes is present in only 16% to 22% of infants with CRS [25].

The teratogenic mechanism of diabetes in CRS is not clear. It has been hypothesized that hyperglycemia leads to release of free radicals from the influx of glucose, across the injured cells and mitochondrial membranes, overwhelming the immature fetal free radical scavenging enzymes. These excess free radicals can be teratogenic either directly or through a chain of events including enhanced lipid peroxidation and prostaglandin imbalance, ultimately leading to disruption in signal transduction [26]. Other proposed factors are hyperketonemia, hypoglycemia, and somatomedin inhibitor excess [15].

The teratogenic insult in diabetic embryopathy occurs from the third to seventh week of gestation at the initiation of organogenesis [27]. The placenta is an effective barrier against maternal insulin, and fetal insulin is not produced before the eighth week of development [28]. Thus, the fetus appears to be vulnerable to hyperglycemic insult during this period. Therefore, stable and good diabetic control in the periconceptional period and throughout pregnancy, particularly during the first trimester, is of paramount importance to prevent congenital malformations. CRS is so specific of maternal diabetes that its diagnosis should immediately lead to screening for this metabolic disorder [11, 18].

Bone scintigraphy is a sensitive procedure for diagnosing skeletal disease and provides valuable information about congenital anomalies of the skeletal system. Although our patient did not have other accompanying abnormalities, in doubtful cases, the sacral area of the bone scan should be carefully examined.

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