Valley sign has been described in patients with Duchenne muscular dystrophy (DMD). As there are genetic and clinical similarities between DMD and Becker muscular dystrophy (BMD), this clinical sign is evaluated in this study in BMD and DMD/BMD outliers. To evaluate the sign, 28 patients with Becker muscular dystrophy (BMD), 8 DMD/BMD outliers and 44 age-matched male controls with other neuromuscular diseases were studied. The sign was examined after asking patients to abduct their arms to about 90° with hands directed upwards; the muscle bulk over the back of the shoulders was observed. The sign was considered positive if the infraspinatus and deltoid muscles were enlarged and between these two muscles, the muscles forming the posterior axillary fold were wasted as if there were a valley between the two mounts. Twenty-five BMD patients and 7 DMD/BMD outliers had positive valley sign. However, it was less remarkable in comparison to DMD. It was absent in all the 44 controls. It was concluded that the presence of valley sign may help in differentiating BMD from other progressive neuromuscular disorders of that age group.

Key Words: Becker muscular dystrophy (BMD), clinical sign, valley sign, muscle hypertrophy, muscle wasting, dystrophin gene, muscular dystrophy

Introduction

Becker muscular dystrophy (BMD) is genetically similar to Duchenne muscular dystrophy (DMD) with gene deletion at Xp 21 locus. The gene product dystrophin, which is a normal component of muscle cell membrane, is absent in DMD but is present in a small amount and in abnormal form in BMD. Perhaps due to this reason the clinical manifestations of DMD and BMD are more or less similar but with a difference that in BMD, the age of onset is late and the progression of symptoms, slow. Among the clinical features, selective muscle involvement is an important characteristic of muscular dystrophies. In DMD and BMD, this selectivity is evident for hypertrophy as well as wasting. In one study done on DMD patients, infraspinatus and deltoid muscles were found to be the second and third most common hypertrophied muscles after the most obvious calf muscles. On observing the wasting, the muscles forming the anterior and posterior axillary folds were found to be the ones most significantly wasted. Still finer observations revealed that in the deltoid muscle, only the central fibers originating from the acromion process were enlarged while the anterior and posterior fibers originating from the clavicle and spinous process of the scapula respectively, were wasted. Similarly, the inferomedial part of the infraspinatus muscle was enlarged while the superolateral part was wasted. In other words, even though the deltoid and infraspinatus muscles were found enlarged, parts of these muscles which traverse through the posterior axillary fold, along with other muscles such as pteres major, pteres minor and latissimus dorsi, were wasted. On the other hand, subtle enlargement of the muscles was found to be best observable when the muscles in question were under mild contraction. Based on these findings, a clinical sign has been described in patients with DMD. The sign which may be called the “valley sign” was observed to be present in about 90% of the DMD patients (BMD and outliers not evaluated). In the present clinical study, this sign was tested in BMD patients and in DMD/BMD outliers, and was compared with other neuromuscular disorders of that age group.

Material and methods

All the patients of BMD and DMD/BMD outliers who attended the outpatient clinic of a Neurology unit in this institution in the last six years and were found to have gene deletion at Xp21 locus, were examined for the “valley sign”. These included 28 patients with BMD from 21 families and eight DMD/BMD outliers from six families. The criteria to call a patient as having BMD included typical history and physical findings of BMD, clinical evidence of gradual progres-
sion of the disease, medical records showing raised serum creatine kinase (CK) levels and myopathic pattern on concentric needle electromyography. Family history of typical progression of the disease and typical histopathological findings in patients or affected siblings, were taken as the definitive evidences whenever present. Gene deletion studies were performed in all patients by the method described in earlier reports. As the muscle biopsy could not be done in all cases and the gene deletion studies yielded positive results in only about two-thirds of the patients, the gold standard for the selection of patients was the positive test for gene deletion at the Xp 21 locus; the rest of them were excluded to avoid any possible contamination from other muscular dystrophies. In the group from which the patients for the present study were selected, about one-third were non-deletional cases6 who were excluded. The patients who were above 16 years of age with no crippling, were included in BMD while those between 12 and 16 years of age who could walk and get up from a sitting position with great difficulty but were not yet chair-bound, were considered as DMD/BMD outliers.

To view the sign, the back of the patient was exposed. He was asked to abduct the shoulders to 90° or thereabouts, with 90° flexion of the elbow, so that the hands were directed upwards. In patients with positive sign, two bulges were visible on either side of a depression on the back of the shoulder, like a valley between the two mounts. The depression or groove ran from the spinous process of the scapula to the posterior axillary fold, such as pteres major, pteres minor, latissimus dorsi and small parts of the deltoid, infraspinatus and long head of triceps muscles. Inferomedial to this depression was the bulge (the mount) due to hypertrophy or relatively preserved bulk of the inframedial two-thirds of the infraspinatus muscle. Superolateral to the depression was the bulge (the second mount) due to hypertrophy or the relatively preserved bulk of the central fibers of the deltoid muscle.

All the 3 components of the clinical sign were analyzed in the patients and the controls. Forty-four patients in the age group of 11-48 (mean + SD = 21.95 + 5.95) years who were suffering from neuromuscular diseases other than DMD/BMD, were also studied for this sign. These included 9 patients with limb girdle muscular dystrophy (LGMD), 8 with spinal muscular atrophy Type III (SMA-III), 9 with chronic polymyositis, 11 with facioscapulohumeral dystrophy (FSHMD) and 7 with myotonia dystrophica. The diagnosis of these patients was supported by clinical, biochemical, electrophysiological and/or histopathological evidences. The sign observed in DMD/BMD patients was compared with the findings seen in these patients. The sign was considered positive only when two independent observers working in Neurology as trainee resident doctors after post-graduate in internal medicine, who were well versed with the sign, agreed with the author’s observation.

Results

All the 28 BMD patients were male in the age range of 17-41 (mean + SD = 21.95 + 5.95) years. All belonged to the central and eastern districts of the Uttar Pradesh province of India. Twenty-six of them had mild to moderate calf muscle enlargement and pure motor gradually progressive proximal muscle weakness; 2 patients had no appreciable calf hypertrophy. The age of onset as told by the patients, was between 11-18 years. All of them presented for the first time at a stage when they had significant weakness in their proximal muscles but all were managing their independent daily routine activity. Their serum creatine kinase (CK) values ranged between 510 IU and 3570 IU. Electromyography (EMG) showed a myopathic pattern in all of them. Nineteen out of the 28 patients had gene deletion at the hotspot, which centered around exon 45 to 51; the rest of them had deletion at other sites in the same Xp21 locus. The valley sign was positive in 25 of 28 BMD patients including the two with inconspicuous calves. All the 25 patients showed enlargement of the deltoid and infraspinatus muscles but the wasting of the posterior axillary fold was less remarkable as compared to the earlier reported DMD cases. The regional topography however, was conspicuous enough to be noticed by an experienced observer as a distinct sign. Out of the 3 BMD cases with negative sign, obesity masked the sign in one, lack of significant wasting of the posterior axillary fold masked it in another and lack of significant enlargement of the infraspinatus muscle masked it in the third patient.

All the eight DMD/BMD outliers were males with the age range of 13-15 (mean + SD = 13.8 + 0.8) years. The age at onset ranged between 6 and 10 years. All of them were able to walk slowly with a waddling gait but had great difficulty in getting up from a sitting position. All of them appeared to be on the verge of becoming chair-bound at the time of examination. EMG showed myopathic pattern in all. Genetic study revealed deletion at the central hotspot in the region of exon 45 to 52 in all the eight cases. The valley sign was positive in seven out of eight cases. In the remaining patient, the wasting of the posterior axillary fold was not significant enough to produce a depression between the two bulges and the bulge formed by the infraspinatus muscle was less remarkable.

Patients of muscular dystrophy other than DMD/BMD and those with SMA-III did not show all the 3 components that were essential to call it a positive sign. However, infraspinatus hypertrophy was observed in two patients with SMA, in one with LGMD and in all the 11 with FSHMD. Also, deltoid enlargement was seen in five patients with SMA-III, one with LGMD, in eight patients with FSHMD and in four patients with myotonic dystrophy.

Discussion

Clinical signs have always played a major role in the diagnosis and management of patients as these cost nothing and depending on specificity, help physicians in reaching the correct diagnosis with fair accuracy. The valley sign is classically described in patients with DMD. The present study is the first to show its presence in BMD and the outliers, which are the milder forms of the same genetic disorder. The value of its presence lies in the fact that several muscular dystrophies and spinal muscular atrophies clinically manifest for the first time...
in adolescence and early adult life and the presence of the valley sign may help in differentiating BMD or the outliers from other related disorders. Though the pattern of muscle involvement helps in clinical differentiation of these disorders, proximal muscle weakness is common to most of them with an exception of myotonia dystrophica. Calf muscle enlargement also helps in differentiating BMD from other disorders, but occasionally, a few patients of LGMD or SMA-III may also demonstrate calf enlargement. Mildly raised CK values also do not help in differentiating these disorders. In this situation, the valley sign may be quite useful in differentiating BMD and outliers from other neuromuscular disorders of that age group.

In DMD/BMD, the selectivity in muscle involvement is so marked that both hypertrophy and wasting could be observed in the same region i.e., on the back of the shoulder. The positive sign which is described as a valley between the two mounts, has three components and all the three must be present to call it a positive sign - (1) Bulge due to hypertrophy or relatively preserved bulk of the deltoid muscle fibers of acromion origin; (2) Linear or oval depression due to wasting of the posterior axillary folds including parts of the deltoid and infraspinatus muscles which traverse the fold and (3) Bulge due to hypertrophy or relatively preserved bulk of the infraspinatus muscle. Thus, wasted posterior axillary fold forms the valley. Superolateral to this valley is seen the deltoid mount and inferomedial to this, the infraspinatus mount. The present study deals with BMD and the DMD/BMD outliers and is an extension of the work done earlier in DMD. Most of the BMD patients were examined at the stage when they were not much crippled. The presence of a positive sign even at this early stage of the disease indicates that the regional topography of the muscles behind the shoulder remains the same in two similar genotypic diseases, i.e., DMD and BMD. However, in BMD the changes in the muscle bulk were less remarkable in the early stage and it reflected in the valley sign, which was also less remarkable in BMD as compared to DMD patients. In this context, we did observe that the valley sign was more remarkable in DMD/BMD outliers whom we examined at the stage of significant disability.

In an analytical account on this new clinical sign, a comparison has been made between this and the Gower’s sign. According to this review, the Gower’s sign is based on selectivity in the loss of muscle power in certain groups of muscles so that the patient makes best use of relatively preserved muscle power (in spared groups of muscles) which can be appreciated in the peculiar way the patient gets up from a squatting position. Thus, one can infer that the Gower’s sign highlights selectivity in the loss of muscle power while the valley sign highlights selectivity in the loss of (or the increase in) muscle bulk. The simplicity in eliciting the valley sign has led to its universal acceptance in DMD and the present study extends its utility to BMD and DMD/BMD outliers.

The present study deals only with the gene deletion positive cases of BMD and DMD/BMD outliers. According to one of our previous studies, this constitutes about two-thirds of all phenotypic cases. In the absence of immunohistochemical studies other cases could not be included but the sign is expected to be positive in some of them also.

Another important observation was the enlargement of both deltoid and infraspinatus muscles in control cases with FSHD. However, the topography in these patients after adoption of the same posture, was so different that this was described separately as a “poll-hill sign”. In FSHD, the trapezius and biceps muscles were found significantly wasted and this was also the case with myotonic dystrophy, but not with BMD or the outliers. Similarly, the observations on the medial border of the scapula were also remarkable. In FSHD, it was directed inferomedially due to inverse rotation and there was winging, predominantly of the inferior angle. In myotonic dystrophy, there was no winging or abnormal rotation of the scapula. In BMD, in spite of minimal winging, there was no inverse rotation and the medial border was directed inferolaterally. If the relatively preserved bulk of the trapezius, biceps and triceps muscles, and normal inclination and slight or no winging of the medial border of scapula, are taken into account, the ‘valley sign’ may be quite useful in differentiating BMD or the outliers from other neuromuscular disorders of that age group. As has been described in patients with DMD, the sign attains greater value by its presence in two BMD patients who had inconspicuous calves.

Acknowledgements

The author gratefully acknowledges the help of Dr. B. Mittal, PhD, Department of genetics, for performing gene deletion studies.

References


Accepted on 15.12.2002