SHORT REPORT

Key words: finasteride; myopathy; side effects; azasteroids

MUSCLE NERVE 20:502–504 1997

REVERSIBLE SEVERE MYOPATHY DURING TREATMENT WITH FINASTERIDE

JOOST HAAN, MD, PhD,[1,2]* JUSTUS M.R. HOLLANDER, PharmD,[3] SJOERD G. VAN DUINEN, MD, PhD,[4] PRAMOD R. SAXENA, MD, PhD,[5] and AXEL R. WINTZEN, MD, PhD[1]

[1] Department of Neurology, Leiden University Hospital, PO Box 9600, 2300 RC Leiden, The Netherlands
[2] Department of Neurology, Rijnland Hospital, Leiderdorp, The Netherlands
[3] Department of Clinical Pharmacy, Rijnland Hospital, Leiderdorp, The Netherlands
[4] Department of Pathology, Leiden University Hospital, Leiden, The Netherlands
[5] Department of Pharmacology, Erasmus University, Rotterdam, The Netherlands

Accepted 1 October 1996

The enzyme 5α-reductase converts testosterone to dihydrotestosterone. 5α-Reductase inhibitors, such as the recently developed 4-azasteroid finasteride, block dihydrotestosterone production and androgen action in the prostate and skin.[5] Treatment with finasteride results in a marked decrease of prostate volume and improvement of symptoms of prostatic hyperplasia.[5] Relatively common side effects of this drug reported so far are decreased libido and impotence. Less than 1% of patients report pelvic or testicular pain, dizziness, headache, asthenia, abdominal pain, diarrhea, flatulence, nausea, rash, or breast pain after treatment with finasteride.[3]

Here, we report a patient with severe but reversible weakness, which we presume to be related to the use of finasteride.

CASE REPORT

A 70-year-old man suffered since 1991 from hesitancy, dribbling, decreased force of urine stream, and incomplete bladder emptying due to benign prostatic hyperplasia. His medical history mentioned cardiac arrhythmia for which no treatment had been given. Since 1992 he used finasteride (5 mg once daily), which had considerably improved the symptoms of prostatic hyperplasia within 1 year. Since 1993, however, he had noticed increasing weakness of both arms and legs. The muscles of arms and legs had markedly decreased in size, and the patient had lost approximately 10 kg of weight during the last 6 months.

The patient never had smoked and used almost no alcohol. In August 1995, he developed dyspnea, had to cough frequently, and had a warm feeling (temperature was not measured). A chest X ray showed a right basal consolidation, and the patient was treated with clarithromycin at home for 10 days. Two weeks later he was admitted because of rapidly progressive weakness and difficulty with coughing.

On admission, general examination showed dyspnea with decreased chest excursions and increased respiratory rate. Temperature was normal. Neurological investigation showed paresis of neck flexors and extensors (4/5), and marked paresis of the arms (proximally grade 2–3/5, distally grade 4/5). The patient could not walk without support due to leg weakness (proximally grade 3–4/5, distally grade 4/5). There was severe generalized muscular atrophy, without fasciculations. Investigation of sensation, reflexes, and coordination was normal.

*Correspondence to: Dr. J. Haan

CCC 0148-639X/97/040502-03

Laboratory investigation revealed normal results of routine hematology and biochemistry, blood gas analysis, lactate dehydrogenase, serum protein spectrum, antinuclear factor, cortisol, serum lactate, cold agglutinins, thyroid function, magnesium, vitamin B12, and vitamin B1. Prostate-specific antigen was 8.0 ng per liter (slightly elevated). On two separate occasions creatine kinase was normal. Administration of neostigmine failed to increase muscle strength. Cerebrospinal fluid examination was normal. Chest X ray now was normal. Electromyography showed polyphasic action potentials with decreased amplitudes in arms and legs, proximally and distally. There was no increment or decrement of the action potential of the abductor digiti quinti on repetitive nerve stimulation. Nerve conduction studies showed lower-normal conduction velocities of arm and leg nerves, with normal compound muscle action potential (CMAP) form and amplitudes. A biopsy of the tibialis anterior showed myopathic signs, but no signs of inflammation (Fig. 1).

We decided to discontinue finasteride because ''asthenia'' has been suggested as one of its possible side effects,[3] although myopathy has never been explicitly reported. Cessation of finasteride medication was followed by a gradual increase of muscle strength, first in the legs, then in the arms. One month after the withdrawal of the drug, the patient was largely improved and dyspnea had disappeared. Muscle strength had improved in arms and legs (proximally to grade 4/5, distally to grade 5/5). At follow-up 1 year later, muscle strength had normalized, and muscular atrophy was less pronounced. Body weight had increased by 5 kg. A second electromyographic investigation, approximately 8 months after stopping the drug, still showed some polyphasy in proximal muscles, but was otherwise normal. The patient was not rechallenged with the drug, because complaints attributable to prostatic hyperplasia had not returned after withdrawal.

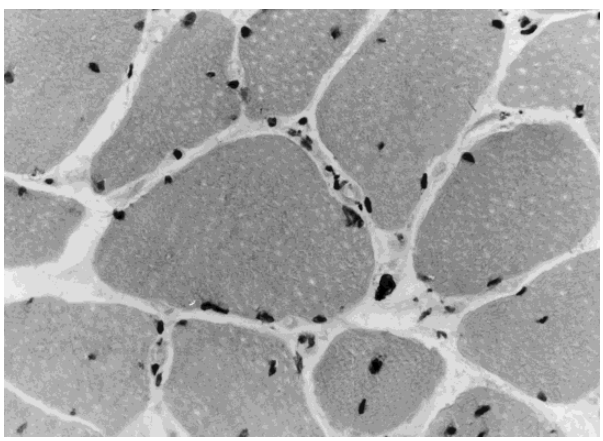

FIGURE 1. Biopsy of the right tibialis anterior (hematoxylin and eosin; original magnification, ×100). A great variation in fiber diameter is seen, with many atrophic and some hypertrophic fibers, and a strong increase of central nuclei.

DISCUSSION

Slowly progressive weakness in an elderly man is a common clinical situation with many diagnostic possibilities.[2] In the present case, the diagnosis of polymyositis was virtually excluded by the finding of normal serum creatine kinase and the lack of inflammation in the muscle biopsy. Amyotrophic lateral sclerosis and progressive spinal muscular atrophy were excluded by the clinical course. The Lambert–Eaton myasthenic syndrome was made unlikely by the severe muscular atrophy, the electromyogram, and the clinical course. Based on the predominantly proximal weakness with muscular atrophy, the electromyographic findings, and the findings in the muscle biopsy, we concluded that the symptoms were caused by myopathy. An intensive search, however, did not uncover a cause for the myopathy. The lack of a different explanation and the improvement after withdrawal of finasteride led us to conclude that this patient had suffered from a toxic myopathy due to this drug.

The enzyme α5-reductase, which is inhibited by finasteride, is not known to be active in muscle. Patients with congenital 5α-reductase deficiency show normal male musculature.[5] This indicates that low or absent 5α-reductase activity, leading to an elevated testosterone level and a low dihydrotestosterone level, does not affect muscular development or function. Therefore, the known pharmacological effects of finasteride do not explain why our patient developed severe toxic myopathy following prolonged use of the drug.

It may be relevant that the clinical features of the myopathy in this case resemble those of glucocorticoid-induced myopathy.[4,6] As in the latter, the clinical course was slowly progressive, was not accompanied by elevated serum creatine kinase, was histologically characterized by atrophy of type II muscle fibers, and resolved after withdrawal of the drug. Further, it is of interest that, as in glucocorticoid myopathy, wasting of muscle tissue was accelerated during an episode of inactivity with a catabolic state.[4] Finasteride is one of the 4-azasteroids, and the parent compound as well as the metabolites have structural resemblance to corticosteroids.[1]

Finasteride-related myopathy must be rare. On the other hand, its widespread use is still short-dated.

We conclude that finasteride should be considered as a causative agent in patients with progressive myopathy.

REFERENCES

1. Carlin JR, Höglund P, Eriksson LO: Disposition and pharmacokinetics of [14C]finasteride after oral administration in humans. *Drug Metab Dispos Biol Fate Chem* 1992;20:148–155.
2. Case report of the Massachusetts General Hospital. *N Engl J Med* 1994;331:528–535.
3. Finasteride, in McEvoy GK (ed): *American Hospital Formulary Service: Drug Information*, Bethesda, MD, 1995, pp 2582–2584.
4. Kaminski HJ, Ruff RL: Endocrine myopathies, in Engel AG, Franzini-Armstrong C (eds): *Myology*. New York, McGraw-Hill, 1994, pp 1726–1753.
5. Rittmaster RS: Finasteride. *N Engl J Med* 1994;330:120–125.
6. Van Balkom RHH, Van Der Heijden HFM, Van Herwaarden CLA, Dekhuijzen PNR: Corticosteroid-induced myopathy of the respiratory muscles. *Neth J Med* 1994;45:114–122.