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Down's Syndrome with Coexistent Gout in 2 Patients: Is the Association Underreported or Is the Prevalence Actually Increasing?

Key Words

Gout
Down's syndrome

Abstract

This report describes 2 patients diagnosed with Down's syndrome and who developed acute gouty arthritis. While hyperuricemia in gout is a well-known abnormality, association of gout with Down's syndrome has not been widely discussed. With increasing life expectancy in this syndrome, it is likely that more such cases will occur. For early diagnosis and proper management clinicians must be aware of this association.

Introduction

Association of hyperuricemia due to decreased uric acid excretion with Down's syndrome is well known [1–4]. Yet, the occurrence of gout in patients with Down's syndrome has not been mentioned in standard textbooks [4, 5]. This association has been described only in case reports [6–10]. Recently, a Japanese group has tried to highlight this association and has given explanations for the rarity of the association in the past and the possible increase in frequency in the present times [11].

In this report we describe 2 patients with Down's syndrome who presented with acute arthritis. In both cases gout was confirmed by

demonstration of monosodium urate monohydrate (MSU) crystals in the synovial fluid of the affected joint.

Case 1

M.H.A.A., a 28-year-old Kuwaiti man, mentally retarded since childhood, was clinically assessed and investigated extensively. The diagnosis of Down's syndrome was made based upon standard clinical criteria. He was repeatedly admitted to this hospital for various medical problems, primarily infections in the throat, chest and skin. However, there were several attacks of swelling in one knee during the past 2 years for which he was given nonsteroidal anti-inflammatory drugs. He was admitted recently with left-sided hemiplegia. Computerized axial tomographic examination of the brain showed multiple areas of small brain infarcts.

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The most recent admission was due to acute painful swellings in the left knee and left 5th proximal interphalangeal (PIP) joint of 2 days' duration. On examination he had an acutely inflamed left knee and left 5th proximal interphalangeal joint. The joints were warm and severely tender. The knee joint had fluctuations indicating the presence of synovial effusion. Investigations showed a normal complete blood count including a normal platelet count and erythrocyte sedimentation rate. Complete serum biochemistry, including liver function tests and renal parameters, were normal. However, the serum uric acid level was 656 $\mu\text{mol/l}$. Serum proteins showed an increase in total globulins of polyclonal variety with reversed albumin to globulin ratio of 34 g/l:41 g/l. The urine examination was normal. The synovial fluid aspirated from the left knee was yellowish and turbid with poor mucin clot and viscosity. White cell count was $31.4 \times 10^9/\text{l}$, and mostly polymorphs. It was, however, sterile. Examination of the synovial fluid under polarized light microscopy showed negatively birefringent needles of MSU crystals diagnostic of gouty arthritis. The patient was given indomethacin 50 mg, 3 times per day after meals which resulted in prompt relief of symptoms in 2 days. He was advised to continue the same medicine for the next 10 days and return for follow-up advice regarding further line of management in 2 weeks. However, the patient did not return for follow-up until the time of this report (10 months since the last visit).

Case 2

J.A.M., a 30-year-old Kuwaiti, was diagnosed with Down's syndrome during early childhood. He had repeated admissions to this hospital with pulmonary infections. He also had one episode of acute ureteric colic. The most recent admission was due to acute onset of pain and swelling in the right knee for 1 day. On examination he had typical clinical features of Down's syndrome. Examination of the right knee showed an acutely inflamed joint which was warm and extremely tender. Fluctuation was demonstrable, indicating the presence of synovial effusion. Investigations showed an increased white blood cell count of $14.4 \times 10^9/\text{l}$, normal hemoglobin, platelets and erythrocyte sedimentation rate, normal serum biochemistry including liver and renal parameters. However, serum uric acid was elevated on two occasions with a reading of 495 and 480 $\mu\text{mol/l}$. Serum proteins showed an increase in total globulins of polyclonal variety with reversed albumin:globulin ratio of 35 g/l:39 g/l. Urine examination was normal. Synovial fluid aspirated

from the right knee was yellowish, turbid with poor mucin clot and viscosity. White cell count was $35.9 \times 10^9/\text{l}$, and mostly polymorphs. It was, however, sterile. Examination of the synovial fluid under polarized light microscopy showed negatively birefringent needles of MSU crystals diagnostic of gouty arthritis. There was a quick response to indomethacin treatment and the patient became asymptomatic within 2–3 days. He was discharged with the advice to take a short course of indomethacin if the symptoms recur and to report to the follow-up clinic. Since then the patient has not had a recurrence of joint symptoms.

Discussion

In both the patients presented in this report, the diagnosis of gouty arthritis was made by demonstrating MSU crystals in the synovial fluid of the affected joint, which is the 'gold standard' for the diagnosis of gout [12]. The most troublesome joint was the knee joint in both patients. This is unusual because in a large majority of patients with gout the first attack involves joints in the foot with about 70% involving the first metatarsophalangeal joint in either foot [12]. The tendency of gout in Down's syndrome to involve the knee joint has been reported by others [7–11]. It would thus appear that knee arthritis in gout occurring in Down's syndrome may be a clinical characteristic of this disease.

The usual age of onset of gouty arthritis in normal population is above 40 years [12]. In contrast, both of our patients were much younger. A younger age of onset of gouty arthritis in Down's syndrome has also been observed in the other reported cases [7–11], the majority presenting with clinical gout in the third decade of life. The reason for this could be the shortened life span in Down's syndrome. Thus, only those with a tendency to develop gout at an early age come to light because those who could have developed clinical gout at a later age do not survive long enough to develop the disease.

Generally, hyperuricemia in Down's syndrome has been reported to be severe [11]. One of the 2 patients presented here had uric acid levels in the 'very high' range, i.e. $>540 \mu\text{mol/l}$ [13, 14]. Yet, the occurrence of gouty arthritis is not common in Down's syndrome. This could be partially explained on the basis of the reported impaired leukocyte function in this disease [15]. The presence of normally functioning leukocytes is necessary for the initiation of inflammation triggered by the presence of MSU crystals [16].

The reason for gout being uncommon in Down's syndrome is probably related to the shortened life span in this disease. In recent times, with improved supportive therapy, the

life expectancy for people with Down's syndrome has increased dramatically [17]. It is therefore expected that more and more patients with this syndrome will present with gouty arthritis. Awareness of this association will help clinicians to consider this diagnosis, confirm it with a simple joint aspiration and examination of the synovial fluid for MSU crystals, and institute appropriate treatment.

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References

- Fuller RW, Luce MW, Mertz ET: Serum uric acid in mongolism. *Science* 1962;137:868-869.
- Kaufman JM, O'Brian WM: Hyperuricemia in mongolism. *N Engl J Med* 1967;276:953-959.
- Nuki G: Disorders of purine and pyrimidine metabolism; in Weatherall DJ, Ledingham JGG, Warren DA (eds): *Oxford Textbook of Medicine*, ed 3. Oxford, Oxford University Press, 1996, pp 1376-1388.
- Wortmann RL: Gout and other disorders of purine metabolism; in Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL (eds): *Harrison's Principles of Internal Medicine*, ed 13. New York, McGraw-Hill, 1994, pp 2079-2088.
- Doherty M: Crystal-related arthropathies; in Weatherall DJ, Ledingham JGG, Warren DA (eds): *Oxford Textbook of Medicine*, ed 3. Oxford, Oxford University Press, 1996, pp 2983-2992.
- Pant SS, Moser HW, Krane SM: Hyperuricemia in Down's syndrome. *J Clin Endocrinol Metab* 1968;28:472-478.
- Cayla J, Rondier J, Auscher C, Perreau C, Gery A de: Goutte et mongolisme: A propos d'une observation. *Rev Rhum Mal Ostéoartic* 1974;41:203-207.
- Nishida Y, Akaoka I, Nishizawa T, Maruki M, Aikawa T, Mitamura T, Yokohari R, Horiuchi Y: A case of gouty arthritis associated with Down's syndrome. *J Ment Defic Res* 1976;20:277-283.
- Ciampi ML, Bazzichi LM, Bertolucci D, Mazzoni MR, Barbieri P, Mencacci S, Macchia De, Mariani G: Uric acid metabolism in two patients with coexistent Down's syndrome and gout. *Clin Rheumatol* 1984;3:229-233.
- Dacre JE, Huskisson EC: Arthritis in Down's syndrome. *Ann Rheum Dis* 1988;47:254-255.
- Kamatani N, Yamanaka H, Totokawa S, Kashiwazaki S, Higurashi M: Down syndrome with coexistent gout: Report of six patients and possible reasons for the scarcity of descriptions of this association. *Ann Rheum Dis* 1996;55:649-650.
- Tate GA, Schumacher HR Jr: Clinical and laboratory features of gout; in Klippel JH, Koopman WJ (eds): *Primer on the Rheumatic Diseases*, ed 10. Atlanta, Arthritis Foundation, 1993, pp 213-219.
- Appendix: Laboratory values of clinical importance; in Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL (eds): *Harrison's Principles of Internal Medicine*, ed 13. New York, McGraw-Hill, 1994, pp 2489-2496.
- Mikkelsen WM, Dodge HJ, Valkenberg H: The distribution of serum uric acid values in a population unselected as to gout or hyperuricemia, Tecumseh, Michigan, 1959-60. *Am J Med* 1965;39:242-251.
- Gregory L, Williams R, Thompson E: Leukocyte function in Down's syndrome and acute leukemia. *Lancet* 1972;i:1359.
- Terkeltaub RA: Pathogenesis and treatment of crystal-induced inflammation; in McCarthy DJ, Koopman W (eds): *Arthritis and Allied Conditions*, ed 12. Philadelphia, Lea & Febiger, 1993, pp 1819-1833.
- Masaki M, Higurashi M, Iijima K, Ishikawa N, Tanaka F, Fujii T, Kuroki Y, Matsui I, Iinuma K, Matsuo N, Takeshita K, Hashimoto S: Mortality and survival for Down syndrome in Japan. *Am J Hum Genet* 1981;33:629-639.