CASE REPORT

Bloom's syndrome in an Indian man in the UK

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SUMMARY

A 17-year-old Indian man was diagnosed with Bloom's syndrome at the age of 3 years. This is the first reported case of Bloom's in an Indian from the UK and the third case report from the British Isles. Bloom's is typically characterised by short stature, photosensitivity, telangiectatic erythema, learning difficulties, immunodeficiency and malignancy. He was born below the 0.4th centile and failed to gain weight as an infant. He presented in clinic with short stature, prominent facial features and hyperpigmented skin patches, which are all defining characteristics of Bloom's syndrome. Other case reports have documented early neoplasms, photosensitivity and learning difficulties in these patients; however, our patient is different, and currently attends a mainstream college, demonstrating little difficulty in coping with the work. To date, he has not presented with any malignancy or characteristic malar rash.

BACKGROUND

Bloom's syndrome is a very rare autosomal recessive condition. It has been shown to commonly occur in the eastern European Ashkenazi Jewish population, which represents approximately one-third of the cases at a 1% carrier frequency.¹ There are also scattered case reports that exist among the Indian population. Parental consanguinity is a common occurrence. Bloom's syndrome is the result of a chromosomal instability disorder caused by a mutation in the BLM gene, which encodes the RecQ helicases. These are a family of proteins that are essential for the structure and integrity of DNA.²

This patient, with an established diagnosis of Bloom's syndrome based on chromosomal studies has, to date, not shown many of the characteristic features reported in other cases, such as neoplasms, severe cognitive impairment, recurrent respiratory infections or photosensitivity. Other case reports on children with Bloom's syndrome have shown that these patients are more prone to develop neoplastic tumours such as Wilms tumour, and that they typically present with a malar rash.³

This case is important because Bloom's syndrome is a rare condition and the symptoms differ from other reported patients with Bloom's. The diagnosis of Bloom's is largely dependent on cytogenetic analysis, as the clinical signs and symptoms vary considerably with only a few examples to learn from in the literature. This case contributes to the limited knowledge surrounding this rare yet serious condition. In previous case reports, patients presented between the ages of 8 and 18 years, whereas our patient was diagnosed at the age of 3 years,

and was managed appropriately with guidance and support available to his family from the onset. Within close proximity to our patient, there were two others patients of the same ancestry but not related, who were also diagnosed with Bloom's syndrome, highlighting the need to consider Bloom's as a differential diagnosis for babies in the Indian population who are failing to thrive.

CASE PRESENTATION

A 1.540 kg male infant was born at term via a normal vaginal delivery to two non-consanguineous Indian parents and was initially admitted to the special care baby unit due to his failure to thrive. Hyperpigmented patches of skin were noted on his limbs from birth. Until the age of 3 years, he had consistently progressed below the 0.4th growth centile. A diagnosis of Bloom's syndrome was made from skin biopsies taken from hyperpigmented patches on his limbs at the age of 3 years. He had no gross abnormalities, and had motor control and reached all his developmental milestones.

At 4 years of age, involvement of a child psychologist concluded that the child would benefit from attending a specialist school as he was 2 years behind children his age. Later, he successfully transferred to a local college where he is currently progressing at the same rate as his peers. Growth hormone treatment was offered at the age of 10–17 years, however, it was refused both times. The boy does not take any regular medication and his vaccinations are up to date. There is no confirmed family history of any genetic conditions.

At present, on physical examination, he shows mild abnormal facial features with a beaked nose, micrognathia and a slender face. He is short in stature and underweight for his age (130 cm; 31.6 kg—below 0.4th centile). He also has several asymmetrical hyperpigmented patches bilaterally on his upper and lower limbs (figures 1 and 2). No telangiectatic erythema can be seen on his face. His voice is of normal pitch and he has no signs or symptoms of malignancy, no respiratory chest infection and no diabetes mellitus.

INVESTIGATIONS

His failure to thrive alongside his hyperpigmented patches provoked cytogenetic testing using a biopsy of these patches. This showed increased frequency of sister chromatid exchange, which was 10 times the normal rate and chromosomal breakage; this is strongly diagnostic of Bloom's syndrome. Throughout his childhood, the boy had undergone regular monitoring of his growth velocity and weight. Routine haematological and biochemical investigations were always normal. He will continue

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Figure 1 Hyperpigmented patch on right calf.

to have blood tests in the future, to provide baseline measurements for anaemia and also establish the level of random growth hormone. He will also require glycated haemoglobin measurements regularly as part of his diabetes mellitus surveillance.

DIFFERENTIAL DIAGNOSIS

The working differential diagnoses were Bloom's syndrome, Fanconi's anaemia, Rothmund-Thomson syndrome and Cockayne syndrome, primarily because of the child's growth retardation and dermatological manifestations. Fanconi's anaemia was excluded due to the absence of heart, lung and gastrointestinal tract abnormalities, bone defects, café-au-lait spots and derangement of cell counts. In Rothmund-Thomson syndrome, there is an increased frequency of sister chromatid exchange, however, it is at a lower level to that observed in Bloom's syndrome, rendering this differential unlikely.

Figure 2 Hyperpigmented patch on right elbow.

Furthermore, there was an absence of juvenile cataracts. Cockayne syndrome is characterised by growth retardation and bird-like facies. However, this child did not display other prominent features such as photosensitivity and pigmentary retinopathy.

We concluded he has Bloom's syndrome based on the cytogenetic analysis showing increased sister chromatid exchange rate combined with growth retardation and hyperpigmented patches, which is diagnostic of the syndrome.

TREATMENT

The boy is currently asymptomatic and being managed conservatively in routine secondary care. His primary treatment will be in the form of regular surveillance for any signs of malignancy and diabetes mellitus. Growth hormone therapy was declined twice due to the patient and his family's perception of its association with malignancy, which is not currently evidence based in this very rare condition. He avoids excessive sun exposure and uses sun screen as he understands he is at high risk of developing skin cancer.

OUTCOME AND FOLLOW-UP

The boy remains at high risk of developing diabetes mellitus, leukaemia, lymphoma and sigmoid colon adenocarcinoma. The mean age of survival is 20.7 years. Men with this condition are also infertile.

He should be treated if he develops symptoms and also be screened for malignancy. He has been advised to avoid sun exposure.

No curative treatment is currently available and surveillance will be the mainstay of his management. He has been offered the option to meet with other Bloom's patients in the local area for further support.

DISCUSSION

Bloom's syndrome is caused by a mutation in the BLM gene, which encodes the RecQ helicases. These are essential for DNA replication and defects in them can cause problems with repairing damaged DNA strands. The deficiency of BLM protein causes the increased rate of sister chromatid exchange as well as increased chromosomal breakage. DNA damage caused by ultraviolet light cannot always be repaired in these individuals, and they are subsequently at high risk of sun sensitivity. The lack of DNA repair is also likely to be the reason for the high incidence of malignancy in these patients as they accumulate mutations. It is surprising that this patient has not reported any symptoms of sun sensitivity or malignancy by the age of 17 years.

The first published case report of Bloom's syndrome was in 1954, in which the patient, born in England and of Jewish descent, presented with growth retardation and a photosensitive facial rash. He suffered from recurrent pyemic abscesses, with one in his ankle resulting in ankylosis.⁴

There are currently only two other case reports from the British Isles: one reported in Ireland in 1983 and the other in London in 2008. The Irish patient died at the age of 4 years, having presented with the key features of telangiectasia erythema, short stature and, eventually, leukaemia. The London case was a 41-year-old woman of Ashkenazi Jewish descent. Similar to our patient, she had a low birth weight of 1.87 kg, below the 0.4th centile, and had characteristic features including a beaked nose and micrognathia. Her intellectual development was not impaired, being in fact above average in her childhood. Her later systemic manifestations of Bloom's included diabetes mellitus, basal cell carcinoma, colonic polyps, osteoporosis,

Patient's perspective

I am now 18 years old. I have had Bloom's syndrome from my birth, which was diagnosed when I was 3 years old. My parents and doctors told me about it but I was too young to understand. Now that I have grown up, I have a better understanding. I know that I will not grow in physical height but I am sure to grow in education. I am prone to catching infections but I have the best family and the best doctors who will always help me in my life. I have enjoyed my life so far with all the special help and care from my family and doctors, including my teachers in school and in college. These people have helped me become the person I am today. I will always remain a special person because of their greatest caring help for me. That is me. Thank you.

Learning points

- ▶ This is the first reported case of Bloom's syndrome in the Indian population in the UK.
- ▶ Bloom's syndrome is a rare autosomal recessive condition that can manifest in a variety of ways.
- ▶ Our patient presented with the classic symptoms of short stature, hyperpigmented patches and prominent facial features.
- ▶ His cognitive abilities are atypical of Bloom's syndrome and he also has shown no signs of malignancy.
- ▶ This case highlights the need to consider Bloom's syndrome as a potential diagnosis in infants presenting with failure to thrive in the Indian population. They may not present with core features such as photosensitivity and malignancy, which have been reported among other populations.

fibrous breast adenoma, cirrhosis and fungal toenail infections. She entered menopause very early in her mid-20s.^{5 6}

Other global case reports have patients presenting with the cardinal features of a photosensitive facial rash in a butterfly distribution, growth retardation, intellectual delays in development and neoplasms.^{7–11}

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REFERENCES

- 1 German J, Ellis NA, Proytcheva M. Bloom's syndrome. XIX. Cytogenetic and population evidence for genetic heterogeneity. *Clin Genet* 1996;49:223–31.
- 2 Hickson ID. RecQ helicases: caretakers of the genome. *Nat Rev Cancer* 2003;3:169–78.
- 3 Cairney AE, Andrews M, Greenberg M, et al. Wilms tumor in three patients with Bloom syndrome. *J Pediatr* 1987;111:414–16.
- 4 Bloom D. Congenital telangiectatic erythema resembling lupus erythematosus in dwarfs: probably a syndrome entity. *AMA Am J Dis Child* 1954;88:754–8.
- 5 Manning DJ, Fennelly JJ, Cahalane SF, et al. Bloom's syndrome: case report. *Ir J Med Sci* 1983;152:108–10.
- 6 Thomas ER, Shanley S, Walker L, et al. Surveillance and treatment of malignancy in Bloom syndrome. *Clin Oncol (R Coll Radiol)* 2008;20:375–9.
- 7 Inamadar AC, Palit A. Bloom syndrome in an Indian child.[Erratum appears in *Pediatr Dermatol*. 2005 May-Jun;22(3):285]. *Pediatr Dermatol* 2005;22:147–50.
- 8 Reddy BS, Kochhar AM, Anitha M, et al. Bloom's syndrome—a first report from India. *Int J Dermatol* 2000;39:760–3.
- 9 Shah H, Sheth FJ, Pandit VS, et al. Bloom syndrome: report of two cases in siblings. *Int J Dermatol* 2013;52:990–2.
- 10 Brassesco MS, Valera ET, Scrideli CA, et al. Bloom's and myelodysplastic syndromes: report of a rare pediatric case with gain of an isochromosome 5p. *Leuk Res* 2012;36:e18–19.
- 11 Festa RS, Meadows AT, Boshes RA. Leukemia in a black child with Bloom's syndrome: somatic recombination as a possible mechanism for neoplasia. *Cancer* 1979;44:1507–10.

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