the zygoma. Autosomal dominant and autosomal recessive types of inheritance have been described. In general, recessive CMD is more severe than the dominant CMD (9).

In none of these disorders, the severity of the illness is as much as in our case. Tallness, bony overgrowth and clinical findings, all were extraordinarily severe in this exceptional case. We searched literature and relevant online sites extensively, but did not find any reported case similar to it. At present we do not know exactly the cause, or genetic background of this rare disorder. Only we can guess that it was because of a new mutation in one of the genes responsible for growth.

Acknowledgements: The authors wish cordially thank to Ghazal Vakili MD, for her kind cooperation in preparing this manuscript, and also, we would like to extend our sincere words of appreciation and gratitude to Mahdi Shafeghati for the invaluable time and effort he kindly put into technically editing this article.

References

1. Daniels GH, Martin JB. Growth hormone excess: Acromegaly and gigantism. In: Isselbacher KJ, Marhn J13. Harrison's Principles of Internal Medicine. Vol 2 13th ed. McGraw Hill; 1994.p.1989-91.

2. Cohen P. Hyperpituitarism, tallstature, and overgrowth syndromes. In: Behrman R, Kliegman R, Jenson HB. Nelson's textbook of Pediatrics. 16th ed. WB Saunders; 2000.p.1685-7.

3. Jones KL. Early overgrowth with associated defects. Syndromes In: Smith's recognizable patterns of human malformation. 5th ed. WB Saunders; 1997.p.150-68.

4. Graham JM. Rimion DL. Abnormal body size and proportion; generalized overgrowth disorders. In: Rimon DL, Conner JM, Pyeritz RE, et al. Emery and Rimoin's principles and practice of medical genetics. Vol. 4th ed. Churchill livingstone;2002.p.1075-77.

5. Sotos J F, Dodge P R, Muirhead D, et al. Cerebral gigantism in childhood: a syndrome of excessively rapid growth with acromegalic features and a nonprogressive neurologic disorder. New Eng J Med 1964;271:109-16.

6. Beckwith J B. Macroglossia, omphalocele, adrenal cytomegaly, gigantism, and hyperplastic visceromegaly. Beckwith J Birth Defects 1969;5:188-96.

7. Savarirayan R, Bankier A. Simpson-Golabi-Behmel syndrome and attention deficit hyperactivity disorder in two brothers. J Med Genet 1999;36:574-6.

8. Johnson JP, Carey JC, Glassy FJ, et al. Marshall-Smith syndrome: two cases reports and a review of pulmonary manifestations. Pediatrics 1983;71(2); 219-23.

9. Sillence DO. Craniotubular remodelling disorders. In: Rimon DC, Conner JM, Pyeritz RE, et al. Emery's and Rimoins principles and practice of medical genetics. 4th ed. Churchill Livingstone;2002.p:4130-5.

10. Ayuk J, Sheppard MC. Growth hormone and its disorders. Postgrad Med J 2006;82(963):24-30.

11. Viljoen D, Beighton P. Marfan syndrome: a diagnostic dilemma. Clin Genet 1999;37(6):417-22.

12. Faravelli F. NSD1 mutations in Sotos syndrome. Am J Med Genet Semin Med Genet 2005;137(1):24-31.

13. Endo F. Berardinelli lipodystrophy syndrome. Ryoikibetsu Shikogun Shirizu 2000; (30pt5):143-4. Review. Japanese.

14. Lachman RS. Skeletal dysplasias. In: Taybi H, Lachman RS. Editors. Radiology of Syndromes, Metabolic disorders, and skeletal dysplasias. 4th ed. Mosby;1996.p.791-802.

of bony calvarium and reduced space for the brain, and the second is being from the proximal part of tibia which is porotic and expanded (figure 4).

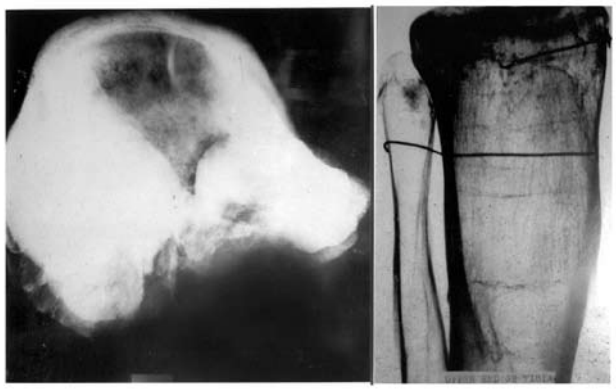


Figure 4: a: lateral view of skull X-Ray. b: Upper part of the tibia and fibula, note to over-expansion of the diaphyseal, metaphyseal, and epiphyseal portions

Discussion

Gigantism is a condition characterized by excessive height growth. The term is applied to those whose height is more than 3 (several) standard deviations above mean for persons of the same age, sex, and ethnic background (1, 2, and 10). For white Europeans and North Americans, the term (gigantism) might be applied to those whose adult height is more than 215 to 220 cm. There are many different disorders that gigantism or overgrowth may be part of their clinical features (3). Pituitary gigantism is very rare, but the most common and pathologically known disease of its type (1, 2, 10). In young persons with open epiphyses, over-production of the growth hormones results in gigantism (10). Its cause is mostly a pituitary adenoma, but rarely hypothalamic or pancreatic tumours that presumably secrete the growth hormone. The hyperplasia of the somatotrophs resulting in hormone release seems to be the main cause of the phenomenon. There are other conditions of overgrowth or excessive tallness in childhood. Simple familial tallness and childhood obesity, precocious puberty and a variety of conditions associated with an excessive amount of testosterone or estrogens in childhood can cause overgrowth(1, 2, and 4). Extra sex chromosomes (47, XXY; 47, XYY; and 47, XXX) usually result in the enhancement of height growth (4). Eunuchoid tallness is because of the hypogonadism and deficiency of sex hormones with long arms and legs. The Marfan syndrome is an uncommon autosomal dominant genetic disease with moderate tallness, arachnodactyly, ocular lens dislocation, and aneurism of the Aorta (11). In Sotos syndrome (Cerebral Gigantism), height is above the 90th percentile in most affected children (12). Macrocrania may also be noted. Most of the patients are mentally retarded with poor coordination. In other overgrowth syndromes like Beckwith-Wiedemann Syndrome(6,3),Simpson-Golabi-Behmelovergrowth syndrome (3, 7), Berardinelli lipodystrophys (13), and Marshal-Smith syndrome (3, 8), clinical findings are quite different from those described for our case. There are some genetic disorders called Craniotubular remodeling disorders (9, 14). The findings and the course of disease in our case are somehow similar to them but extremely more severe. These disorders are a large group characterized by abnormal modelling as well as increased bone density. Diaphyseal displasia, Craniodiaphyseal dysplasia, Pachydermoperiostosis, and Frontometaphyseal dysplasia are some examples.

Craniodiaphyseal dysplasia (CDD) is a rare craniotubular remodelling disorder with hyperostosis and sclerosis of the skull and facial bones, along with hyperostosis and defective remodelling of the shaft of the tubular bones. The epiphyses and metaphyses are only mildly affected. Pachydermoperiostosis is an unusual condition. Acromegaly has been described in association with radiological findings that are similar to hypertrophic osteoarthropathy. Frontometaphyseal dysplasia (FMD) causes a striking facial appearance with a Taurus-like bony overgrowth of the frontal bones. In Craniometaphyseal dysplasia (CMD), there is progressive facial dysmorphism with a broad osseous prominence of the nasal root extending across

in the history of medicine. So, he decided to preserve the patient's body instead of having him buried. After a few years, the patient's family returned to their home village, and the body of the proband was transferred to the anatomy department of the Medical School, where all his soft tissues and internal organs were removed, and his skeleton, after processing, was placed as a single piece of heavy wood that stands in the entrance hall of the University (figure 2). At present, the frightening monstrous giant is standing there firmly and respectfully saluting ordinary visitors, researchers, and simply, anyone who would like to get acquainted with one of the very extraordinary creatures of God!

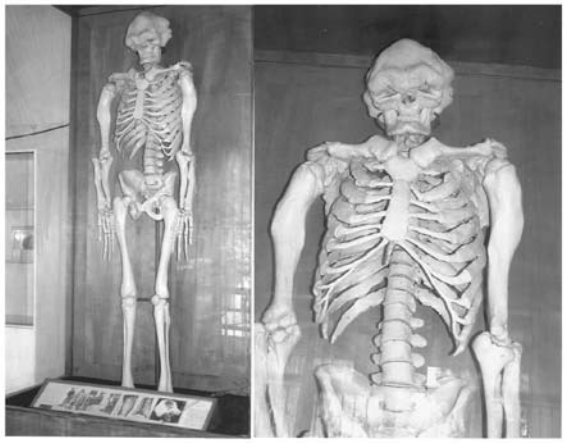


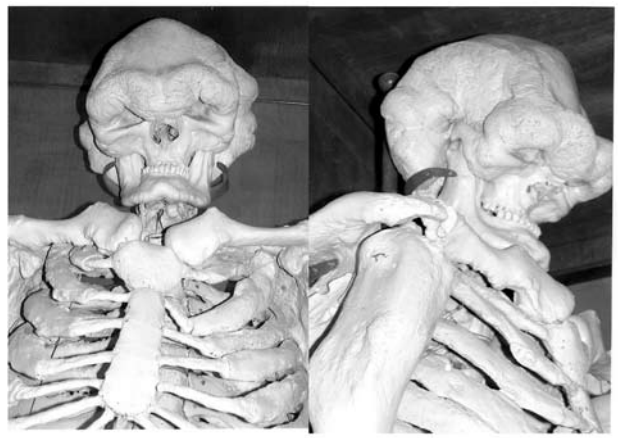
Figure 2: a: Complete skeleton of Siah-Khan, standing in the Entrance Hall of Shiraz Medical Science University.b: Close up view of the upper part of the skeleton

Cardinal clinical findings

- Height was 259 cm; and weight 250 kg.
- Severe mental retardation.
- Very unusual behavioural problems.
- Uncontrollable and unreserved sexual desires.
- Precocious Ageing.
- Inability in standing up from a sitting position.
- Inability in bending and turning to the right or left.
- Prognathism due to mandibular overgrowth.
- Strange facial features because of bony projection on frontal bone.
- Occipital bone growing backward.
- Frontal bone growth progressing to the forward and downward of the eyes as a thick wall limiting the field of vision just like a front porch.
- Large hands with long fingers.
- Large feet, very flat feet, bumping steppage.
- Great appetite as much as 3 to 4 people with good appetite.
- Looking like a strong, dry piece of thick wood and unable to move in different directions because of the fast growth of bones and early vertebral body fusion (Figures 1،2)

Skeletal abnormalities

Figure 3 show the patient's skeletal anomalies. The height of the skeleton is 259 cm; the lengths of the upper extremities were 117 cm, and the lower extremities 125 cm. The very severe overgrowth in calvarial bones, clavicles, scapulae, long tubular bones, ribs, and pelvic bones are apparent.



Figures 3: You can see extensive bony overgrowth in the skull, facial, clavicular, scapular, ribs, and humerus bones.

X-Rays

Only two photos of X-Ray films are available: a lateral skull X-Ray which shows severe overgrowth

Introduction

Gigantism is a condition characterized by excessive height growth. The term has typically applied to those whose height is several standard deviations upper than the normal population (1). The most common cause of pathologically tall stature is pituitary gigantism. The excessive growth hormone, usually results from over-secretion by a group of somatotrope cells of anterior pituitary gland (somatotrope adenoma). The primary effect of the disease is excessive growth resulting in tallness (1, and 2). Tallness is accompanied by heavy, thick bones with large hands and feet and a heavy jaw. Once puberty is complete and adult height achieved, continued growth results in acromegaly. In this case diagnosis is not so difficult. By measuring blood growth hormone (GH) and insulin like growth factor 1 (IGF1), clinical impression can be confirmed. There are some other very heterogeneous and very rare genetic and non-genetic conditions that overgrowth or tallness is a consistent finding in them (3, 4); such as Precocious puberty, Extra sex chromosome syndromes (4), Sotos syndrome (3, 5), Beckwith-Wiedemann syndrome (3, 6), Simpson-Golabi-Behmel syndrome (3, 7), Marshal-Smith syndrome (3, 8), and some of the Craniotubular Dysostoses (3, 9, 14).

We report here an Iranian patient who was living in early 20th century (1912-1940) in the southern city of Shiraz. Clinical features on him, especially, very extreme tallness, skeletal overgrowth, mental and behavioural symptoms were quite different from the mentioned disorders. This case, to the best of our knowledge, is a unique one, and not any similar version has ever been reported in world medical publications to date.

Case Report

In a village called Lapouee located within about 50 km to the south of Shiraz, the capital of Fars Province, a boy was born in 1912 through normal vaginal delivery.

He was the third child of a poor farmers' family. His two older siblings were healthy. The parents were healthy as well. The growth and development of the proband were reported as normal by the age of 6. Then a very rapidly progressive growth-spurt occurred in him. He looked like a 20-year-old man when he was only 9 years old. His family moved to Shiraz because of financial problems and his very strange and mysterious illness at the age of 9. Gradually his appearance changed to a terrifying monstrous giant (figure 1). It is quite clear that his appearance was similar to an old man, and deformities on his skull, face, upper and lower extremities were extremely unusual (figures 1). In 1922, Prof Ghorban, the founder and first president of Shiraz University of Medical Sciences got acquainted with him. He frequently visited the case, helped the family by offering necessary medical services, and supported them financially. Because of the many difficulties in managing the patient by his family, Prof Ghorban decided to hospitalize him in Saadi Hospital, one of the city's Medical School's affiliations. He was kept there until the age of 28, when he died of pneumonia and sepsis in 1940.

Figure 1: Left to right; a- Siah-Khan when he was 13 years old. b Siah-Khan in age 18. and c: the monstrous giant in age 23.

Prof. Ghorban knew that his patient was one of the very extremely rare and perhaps precious creatures

Case Report

Cranio-Spondylo-Tubular Dysostosis A Unique Historic Iranian Giant "Siah-Khan Syndrome" Report of an extremely rare or perhaps a unique case in the world from Iran

Mohammad Hassan Sheikholeslami[1], Yousef Shafeghati[2,3*]
Zabihollah Ghorban[4]

1-Retired Prof. of Pathology, Shiraz Medical Sciences University; Shiraz, Iran
2- GRC, University of Welfare Sciences & Rehabilitation, Evin, Tehran, Iran
3- Medical genetics Department, Sarem Women Hospital, Shahrake Ekbatan, Tehran Iran
4- Founder and first president of Shiraz Medical Science University, Shiraz, Iran

Severe overgrowth and tallness is very rare in human beings. The most common cause is gigantism due to the excessive secretion of the growth hormone, especially, before the closure of long bones' epiphyseal growth plates. There are other rare disorders that are categorized on overgrowth syndromes. Herein, we report an extremely rare, or even perhaps a unique, patient from Iran. The clinical and skeletal findings were very unusual, with extensive clavarial, tubular, vertebral, ribs, and scapular overgrowth and synostosis. Indeed, the results of these abnormalities made a monstrous giant with a very tall stature. This is a unique case, which was living during 1912-1940 in Shiraz. The report's information and photos, kindly supplied by Prof. Sheikholeslami. We evaluated thoroughly the findings together. Now we think; this is a very unusual case of its type, perhaps a Craniotubular Dysostosis Syndrome. We searched medical and clinical genetics literature, but did not find any similar case, having been reported before. So, to our knowledge, this is a unique case in the history of world medicine. We suggest to call this entity; "Siah-Khan syndrome" (after the patient's name), or " Ghorban-Sheikholeslami-Shafeghati syndrome" (in honour of Prof. Ghorban who was recently has died, or " Cranio-Spondylo-Tubular Syndrome".

Keywords: Siah-Khan Syndrome, Ghorban-Sheikholeslami-Shafeghati Syndrome, Cranio-Spondylo-Tubular syndrome, extremely severe monstrous giant.

* **Yousef Shafeghati, MD**
E.mail: y_shafeghati@yahoo.com Tele-fax: +98(21)44 633 283
Submission date: 4/9/2010 Acceptance date:1/11/2010