Case Report

Rapid progression of scoliosis curve in a mature patient with undiagnosed pituitary macroadenoma: A rare case report

Weng Hong Chung, Chee Kidd Chiu, Chris Yin Wei Chan, Mun Keong Kwan

Department of Orthopaedic Surgery (NOCERAL), University of Malaya, School of Medicine, Kuala Lumpur, Malaysia

ABSTRACT

Growth hormone secreting pituitary tumor or gigantism has not been previously reported to be associated with rapid progression of scoliosis in the literature. However, there are some reports indicating scoliosis can be worsened by growth hormone therapy in children and adolescents. A 19-year-old boy was referred to our institution for the treatment of a right thoracolumbar scoliosis. The Cobb angle had worsened from 29° to 83° over two years' duration. He attained puberty at the age of 13. He had a previous history of slipped upper femoral epiphysis (SUFE), which was operated in 2015, with no clinical features of gigantism. Preoperative assessment was performed. He was diagnosed with growth hormone secreting pituitary macroadenoma by magnetic resonance imaging with a high serum level of insulin-like growth factor-I (IGF-I). Computed tomography (CT) of the pancreas showed a pancreatic endocrine tumor. The patient was later diagnosed with multiple endocrine neoplasia type 1 (MEN 1). He underwent endoscopic endonasal excision of the pituitary mass and distal pancreatectomy. This case indicates that growth hormone secreting pituitary macroadenoma could result in rapid progression of scoliosis.

Introduction

Maximal curve progression occurs after the peak growth spurts and extends one and half years further until skeletal maturity is achieved (1). Worsening of scoliosis after skeletal maturity is associated with syndromic conditions, disc degeneration, facet joint arthritis, and wedging of the disc spaces.

Pituitary adenoma (PA) accounts for 10-15% of all intracranial tumors and its presentation depends on the nature of the hormones involved (2). Rapid progression of scoliosis has not been reported to be associated with growth hormone (GH) secreting pituitary macroadenoma. Therefore, we would like to report a rare case of undiagnosed pituitary macroadenoma where the patient presented with rapid progression of a right thoracolumbar scoliosis.

Case Presentation

A 19-year-old boy was referred to our institution for the treatment of a right thoracolumbar scoliosis. At the age of 17, his Cobb angle was 29° (Figure 1. a, b). He was treated conservatively with back strengthening exercises and back care. Bracing was not instituted at this stage. The scoliosis gradually worsened to 65° by the age of 18 despite the fact that his skeletal maturity was at Risser stage 5 at that point (Figure 1. c, d). He was advised for corrective surgery but was not keen for surgical intervention at that point. A year later, the scoliotic curve further deteriorated to 83° (Figure 1. e, f). Due to the rapid worsening of his curve, he decided to proceed with surgical intervention. Past surgical history revealed that he had surgery for a slipped upper femoral epiphysis (SUFE) in 2015. Medical history was not remarkable. He attained his puberty, i.e., change of voice at the age of 13.

On clinical examination, the patient had a tall stature with a height of 184 cm, arm span of 192 cm, body weight of 65 kg, and body mass index of 19.2 kg/m². Arm span to height ratio was 1.04. He had reached Tanner stage 5. There were no other syndromic features, neurocutaneous stigmata, or signs to suggest spinal dysraphism. He had a stooped posture, neck tilt, marked prominence of the right rib cage with waistline asymmetry, and leg-length discrepancy of 3 cm (Figure 2). Cardiac, respiratory, and neurological examinations were not remarkable.

Complete blood count showed thrombocytopenia and liver function tests showed high serum alkaline phosphatase (Table 1). Supine side bending radiographs are shown in Figure 3. The magnetic resonance imaging (MRI) of the whole spine did not show any spinal anomaly; however, we noticed an intracranial soft tissue shadow at the edge of the sagittal image of the MRI of the spine. A suspicion of an intracranial tumor was raised; therefore, we proceeded with an MRI of the brain which demonstrated a pituitary macroadenoma (Figure 4). Subsequently, a hormonal study was performed and showed increased levels of serum insulin-like growth factor-I (IGF-I) (Table 1). Computed tomography (CT) of the pancreas was performed when he experienced symptoms of hypoglycemia, and it showed a pancreatic endocrine tumor (Figure 5). The patient was later diagnosed with multiple endocrine neoplasia type 1 (MEN 1) and eventually underwent an endoscopic endonasal excision of the pituitary mass and on a later date, a distal pancreatectomy. The histopatholog-
ical examination (HPE) of the pituitary mass revealed a mixed function (predominantly GH) pituitary adenoma while the HPE of the pancreas reported a pancreatic neuro-endocrine tumor which was consistent with an insulinoma (Figure 5). As a sequela of the pituitary excision, he developed panhypopituitarism with the following abnormalities: Thyroid stimulating hormone (TSH) 0.26 mIU/L (reference range 0.55-4.78 mIU/L), IGF-I 66 ng/mL (reference range 117-323 ng/mL), cortisol 36 nmol/L (reference range 145-619 nmol/L), follicle stimulating hormone (FSH) 0.8 IU/L (reference range 1.4-18.1 IU/L), and testosterone <0.2 nmol/L (reference range 5.72-26.14 nmol/L). He was treated with intra-muscular injection of testosterone 250 mg monthly, oral prednisolone 5 mg twice daily, oral levothyroxine 100 mg once daily, and desmopresin 0.1 mg twice daily. He was planned for scoliosis surgery as soon as his condition and hormonal imbalance was optimized.

Discussion

PAs have a prevalence of 80-90 cases per 100,000 of the population, accounting for approximately 15% of intracranial tumors (3). They have a variety of biological behaviors according to their distinct histopathological location and the different types of cellular origins within the pituitary gland. About two-thirds of PAs may secrete excess hormones and 8 to 16% of PAs were secreting GH (4).

| Table 1. Blood investigation results |
|-------------------------------------|
| **Test**               | **Unit** | **Reference Range** | **Flag** | **Result** |
|------------------------|----------|---------------------|----------|-----------|
| Hemoglobin             | g/L      | 130.0-170.0         | 137      |
| White Blood Count      | 10^9/L   | 4.0-10.0            | 4.1      |
| Platelet               | 10^9/L   | 150-400             | L        | 107       |
| Alkaline Phosphatase   | U/L      | 45-129              | H        | 176       |
| Complement 3           | mg/dL    | 90-180              | 100      |
| Complement 4           | mg/dL    | 10-40               | 19       |
| Anti-Nuclear Factor    |          | negative            |          |
| Anti-dsDNA (ELISA)     | IU/mL    | 0-200               | 171      |
| Rheumatoid Factor      | IU/mL    | <15.9               | <11      |
| Free T4                | pmol/L   | 11.5-22.7           | 17.6     |
| Thyroid Stimulating Hormone | mIU/L | 0.55-4.78      | 2.07     |
| Insulin-like Growth Factor-I | ng/mL | 173-414        | H 452    |
| Cortisol               | nmol/L   | 145-619             | 469      |
| Luteinizing Hormone    | IU/L     | 1.5-9.3             | 2.3      |
| Follicle Stimulating Hormone | IU/L | 1.4-18.1    | 3        |
| Prolactin              | mIU/L    | 45-375              | 432      |

Anti-dsDNA: anti-double stranded DNA antibody; ELISA: enzyme-linked immunosorbent assay

Figure 1. a-f. Posteroanterior and lateral standing radiographs of the spine from 2016 (a and b), 2017 (c and d), and 2018 (e and f) showing increase of the Cobb angle (T1-T9 and T10-L3 levels) in the past three years. The white arrows show Risser stage 4 in Figure 1a and stage 5 in Figure 1, c, e

Figure 2. a-c. Clinical photographs from the front (a), back (b), and side (c) show a severe thoracolumbar scoliosis with neck tilt, right rib cage prominence, waistline asymmetry and leg-length discrepancy of 3 cm

HIGHLIGHTS

- Growth hormone secreting pituitary tumor or gigantism has not been previously reported to be associated with rapid progression of scoliosis in the literature.
- A 19-year-old boy presented with a rapidly progressing thoracolumbar scoliosis (Cobb angle worsened from 29° to 83° over two years’ duration).
- He was diagnosed with growth hormone secreting pituitary macroadenoma by magnetic resonance imaging with a high serum level of insulin-like growth factor-I. Computed tomography of the pancreas showed a pancreatic endocrine tumor. The patient was later diagnosed with multiple endocrine neoplasia type 1 (MEN 1).
In fact, GH is important for skeletal growth and the attainment of adult height and is mainly regulated by somatostatin and GH-releasing hormone, but also by signals from the periphery, such as ghrelin and by feedback inhibition via IGF-1. Chronic hypersecretion of GH leads to increased IGF-1 production by virtually all organs and tissues, thereby increasing somatic and visceral growth even after skeletal maturity. This could probably explain the rapid progression of scoliosis in our patient even after skeletal maturity. High serum GH
levels cannot promote growth in the absence of IGF-I generation as witnessed by the dwarfism in patients with genetic mutations of GH receptors (Laron’s Syndrome) [5].

Gigantism has distinct clinical features, such as broadened hands and feet, stubby fingers, widened nose, bulging forehead, thick lips, obvious cheekbones, and marked facial lines. The clinical features of gigantism described in the literature do not include rapid progression of scoliosis. However, our patient who was diagnosed to have PA by high levels of IGF-I, did not have the distinct features of gigantism.

There was limb length discrepancy (LLD) of 3 cm in our patient. A patient with LLD could have a compensatory scoliotic curve if the LLD was significant. Usually, a patient with a short left lower limb will have a compensatory left thoracolumbar/lumbar (TL/L) curve. However, in our patient, the curve was a right-sided TL/L curve. Therefore, we think that the occurrence of both LLD (shorter left lower limb) and a right-sided TL/L curve could be coincidental.

To our knowledge, there is no English literature associating GH secreting PA and scoliosis. However, scoliosis was commonly reported as one of the orthopedic adverse effects of GH therapy. In 1978, Dymling and Willner were the first to report the progression of a structural scoliotic curve in a patient, who was previously diagnosed with panhypopituitarism, during GH treatment [6]. In 2001, the Growth Hormone Research Society conducted a study stating that scoliosis can be exacerbated as GH therapy can accelerate growth [7]. Furthermore, in a study by the National Cooperative Growth Study (NCGS), 238 out of 54,996 patients on GH had scoliosis, of which 76 had progression of pre-existing scoliosis [8]. In some syndromic conditions, such as Turner syndrome and Prader-Willi syndrome, GH therapy can pose an additional risk of scoliosis [9, 10]. Wang et al. screened 250 patients who were undergoing GH therapy and found that 10 patients developed scoliosis, of which 6 required orthoses due to curve progression [11].

Conclusion

Rapid progression of scoliosis is considered as an unrecognized skeletal condition in patients with GH secreting pituitary macroadenoma. This case illustrated that the progression of scoliosis can be aggravated without any distinct clinical presentation of gigantism.

Informed Consent: Written informed consent was obtained from the patient who participated in this case.

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