

Growth hormone therapy in boy with panhypopituitarism may induce pilomatricoma recurrence – Case report

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Abstract

Pilomatricoma is usually a solitary subcutaneous nodule. Recurrence of the nodule after surgical excision is very rare. Pilomatricoma occurrence in patients with growth hormone (GH) deficiency has not been reported, yet. We report a 14-year-old boy with pilomatricoma and panhypopituitarism. After GH therapy had been started, we observed two relapses of previously completely excised pilomatricoma in the same location and a new pilomatricoma formation on the chin.

INTRODUCTION:

Pilomatricoma, also known as calcifying epithelioma of Malherbe, is a benign tumour of hair matrix cells [1]. It is the second of the most common superficial tumour excised in children with 40% of lesions occurring in patients under the age of 10 years [2]. Patients usually experience solitary nodule, whereas multiple lesions may be associated with other diseases: myotonic dystrophy (Steinert's disease), sarcoidosis, Gardner's syndrome, Rubinstein-Taybi syndrome and Turner's syndrome [3–5]. Multiple pilomatricomas were found in 2–10 % of reported cases [4]. Recurrences after surgical excision are rare, with an incidence of 0–3 % [2–3].

We report a 14-year-old boy with ectopy of posterior lobe of pituitary gland treated with growth hormone (GH) and L-thyroxine and multifocal

form of pilomatricoma. Lesion localized on the left cheek recurred twice in 5 months after its surgical excision.

OBSERVATIONS:

14-year-old boy, from 4 years of age suffered from solitary, hard and painful on palpation nodules, 5–20 mm in diameter, occurring in intervals of 2–5 years time in different regions of the body (6 nodules in total), localized initially on the trunk (in the interscapular region – 2 nodules), upper extremities (left arm – 1 nodule, left forearm – 1 nodule) and then on the face (right cheek – 1 nodule) and neck (1 nodule). His family history was unremarkable. Histopathological examination of excised nodules showed epithelioma calcificans Mal-

herbe (pilomatricoma) excised with healthy tissue margin in all cases (Fig. 1).

Considering his extremely short stature (height SDS= -3,0), 50% delay in bone age (bone age 3,5 years, calendar age 7) and low growth velocity (3–4 cm/year) the boy was followed-up by the endocrinologist. When he was 7 years old, secondary hypothyroidism was diagnosed (fT4: 0,63 ng/dl, normal range: 0,89–1,8 ng/dl; TSH: 1,2 uIU/ml, normal range: 0,32–5,5 uIU/ml) and L-thyroxine was administered. Growth hormone deficiency (maximal GH releases up to 2,5 ng/ml in 2 stimulatory tests after insulin and clonidine challenge, normal range: > 10 ng/ml; low IGF-I: 64,25 ng/ml; SD= -4,04) was stated when he was 14 years old. MRI scan revealed ectopy of posterior lobe of pituitary gland. These indicated growth hormone therapy to be started. During 14 months of GH administration (0,65 IU/kg/week) patient's height increased by 14 cm. Very good height velocity (HV=1 cm/month) and increase of serum IGF-I concentrations to 694,4 ng/ml (SD=2,19) and 1014,09 ng/ml (SD=3,46) after 6 and 14 months of GH therapy, respectively confirms the efficacy of growth hormone therapy in our patient.

Considering supraphysiological serum concentrations of IGF-I, we decided to cut down the dose of GH to 0,55 IU/kg/week, observing the return of IGF-I serum concentration value to physiological value (508,96 ng/ml; SD=0,97).

All IGF-I SD values were calculated according to Löfqvist et al. [6].

Before GH therapy was started, all pilomatricoma nodules had been completely excised. After 6 months of GH administration, solitary nodule on the left cheek, 2 cm in diameter occurred, that was completely excised. After the next 3 months of GH administration the nodule on the left cheek relapsed in the same location. The nodule was excised with the margin of healthy skin (confirmed in histopathological examination). Two months after its re-excision we observe second relapse of the nodule in the postoperative scar and new nodule formation on the chin (Fig.2).

DISCUSSION:

First pilomatricoma nodule in our patient appeared at the age of 4 years old, that is a typical time to diagnosis of such skin lesions. Julian and Bowers [7] reported the peak age of presentation is 5 to 15 years in female and up to 5 years in male patients. There is also a second peak in adults between 50 and 65 years of age. According to the others [4] the most of cases occur between 8 and 13 years of age. The female-male ratio ranges from 0,43:1 to 3:2, but a female preponderance is noted in a majority of the studies [3,7].

Anatomical location of the nodules in our patient is typical for pilomatricoma, although the first lesion occurred on the trunk (in the interscapular region), not on the head. In 40–70% of cases tumors are located on

the head, predominantly in frontal, temporal areas and on the cheeks. Only in 9,5 % pilomatricomas are found on hair-bearing parts of the head despite pilomatricoma arises from follicle matrix cells because their density is even twice more on the face than on the hair-bearing skin of the head [2]. In 35,5 % of cases the tumors occur on upper extremities, in 4% on lower extremities and in 4% on thorax [7]. Pilomatricoma does not appear on palms, soles and genitals [7].

Pilomatricomas are usually solitary nodules. In our patients, single nodules occurred in different regions of the body in intervals of 2–5 years time, that suggests multifocal lesions. This form of pilomatricoma was reported by others with concomitant myotonic dystrophy or other diseases [2,4]. Our patient has panhypopituitarism due to ectopy of posterior lobe of the pituitary gland and needs to be treated with growth hormone. Coexistence of these two conditions has not been reported, yet.

It should be noted, that in our patient, we observed two relapses of nodule located on the cheek, in postoperative scar soon after growth hormone therapy has been started. Recurrences of pilomatricoma after surgery are very rare (0–3%), and a diagnose of pilomatricoma should be taken into consideration [2,3]. However, histopathological examination excluded pilomatricoma or multinodular pilomatricoma, reported by others [8].

Animal studies, as well as clinical studies in human demonstrated that growth hormone therapy may in some cases increase the risk of cancer development *de novo* or second neoplasm or tumor recurrence in those previously treated for a malignancy [9–11]. Growth hormone and its effector hormone – insulin-like growth factor (IGF-I) mediating mitogenic and anabolic effects, may stimulate proliferation of normal and malignant cells [9]. Epidemiological studies indicated an increased risk of colorectal cancer in patients with acromegaly [11], however serum GH and IGF-I concentrations are markedly elevated in these patients.

On the other hand extensive studies of the outcome of GH replacement therapy in childhood cancer survivors showed no evidence of an excess of *de novo* cancers and there is no evidence whether GH in modern dosage regimens is associated with an increased risk of colorectal cancer [11,12]. Despite early concerns following a report of a cluster of cases of leukaemia in recipients of GH, there appears to be no increased risk for the development of leukaemia in those treated with GH unless there is an underlying predisposition. Even in children with a primary diagnosis of cancer, subsequent GH use does not appear to increase the risk of tumour recurrence [13]. Only in one study an increase of second neoplasms in cancer survivors who also received GH therapy was demonstrated with a tendency to diminish with increasing length of follow-up [14]. Many authors emphasise that children with somatotropin deficiency are treated with replacement, physiolog-

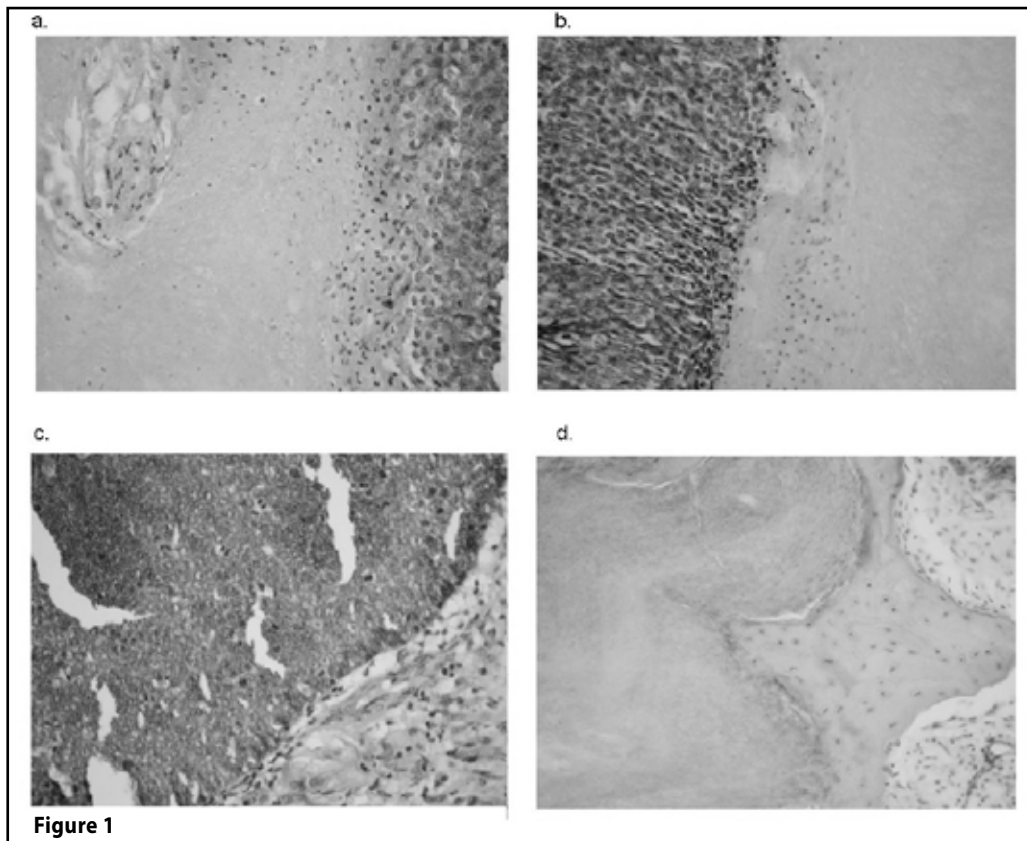


Figure 1

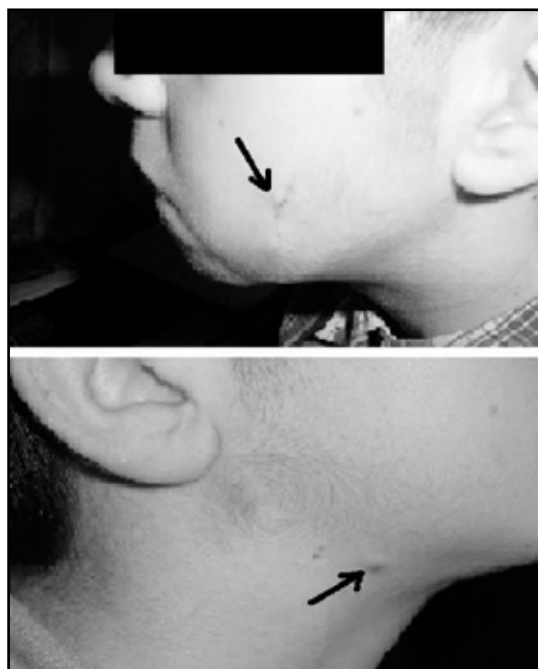


Figure 2

Figure 1 (above). Histopathological examination of pilomatricoma

- The rim of basaloid cells on right. The central portion of tumor composed of cornified material with shadows cells (ghost) cell. H&E; 200x.
- The retained nuclei in the transition zone between proliferating basaloid cells on the right and cornified material with shadows cells on the left. H&E; 400x.
- The mitotically active proliferating basaloid cell in the recurrent tumor. H&S; 200x.
- Confluence osseous metaplasia in the recurrent tumor. The shadows cells on the left lie close with metaplastic bone on the right. H&E; 400x

Figure 2 (left). Relapse of pilomatricoma nodule in the postoperative scar after pilomatricoma excision on the left cheek in 14-year-old boy treated with growth hormone due to panhypopituitarism and a new pilomatricoma formation on the chin in the same boy.

ical doses of growth hormone, not exceeding physiological levels [11,15]. It should be noted, however that in our patient growth hormone therapy caused an increase of IGF-I serum concentrations from very low to supraphysiological values.

It has been also demonstrated that IGF-BP-3 inhibiting IGF-I proliferatory action and inducing apoptosis on caspase-independent mechanisms may play a role of

preventive factor in cancer development. and the cancer risk is increased in individuals in whom both high IGF-I and low IGF-BP-3 are present. GH treatment induces both IGF-I and IGF-BP-3 concentrations rise and these patients are not within elevated cancer risk [15] Unfortunately IGF-BP-3 serum concentrations in our patient were not assessed.

We suggest that considerable increase of serum IGF-I concentrations from very low to supraphysiological values in a short time may induce pilomatricoma recurrence in our patient. This supports a need of IGF-I measurement in optimizing GH dosing that should be preferably kept within normal age-related ranges.

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