

Longitudinal study of behavioral and affective patterns in girls with central precocious puberty during long-acting triptorelin therapy

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ABSTRACT

The aim of the present study was to evaluate the behavioral and affective characteristics and the changes in psychosocial functioning resulting from precocious puberty in 15 girls with central precocious puberty treated for 2 y using the GnRH agonist long-acting triptorelin, and in 5 untreated girls. After diagnosis of precocious puberty at 6.6–10.4 y of age, height, weight and pubertal development were evaluated at 3-month intervals over 2 y. Semi-structured interviews were carried out with the patient, the parents and the pediatric endocrinologists at 1, 8, 16 and 24 months after diagnosis. Standardized questionnaires (Child Behavior Checklist, Self-esteem Inventory) were administered at 1 and 24 months or 16 and 24 months, respectively. There was a mean 1,5-y delay between the observation of signs of puberty as reported by the parents and the diagnosis of precocious puberty at the first consultation of a pediatric endocrinologist. Before follow-up, all 20 girls were very concerned about physical differences from peers, particularly breast development. During therapy, breast regression to minimal or absent development occurred in 5/15 treated patients, who then no longer felt embarrassed about pubertal development in contrast to the other patients. Fear of sexuality remained obvious throughout the study in most patients. Feelings of loneliness and exemplary behavior were observed and tended to decrease in the treated patients and to increase in the untreated patients. Elevated scores of withdrawal, anxiety/depression and somatic complaints at Child Behavior Checklist were still observed after 2 y. These changes in behavioral and affective characteristics appeared to be related neither to height and weight, nor to development of pubic hair, which progressed in most patients. After 2 y, the physical differences remained a concern for 13 girls and the risk of short adult stature for 6. In summary, some behavioral and affective characteristics and particularities in psychosocial functioning are observed in girls with precocious puberty. During treatment with long acting triptorelin, problematic behavior and functioning decrease slightly, particularly in the few girls showing breast regression to minimal or absent development.

Since gonadotrophin-releasing hormone (GnRH) agonists have been proposed for the treatment of central precocious puberty (CPP) (1), such treatment has proven to be very effective in causing reversible pituitary-gonadal suppression (2, 3). In the long-term, the purpose of GnRH agonist therapy is to prevent the early fusion of bone epiphyses and the resulting short stature. This issue has been quite extensively studied and some possible effects on adult stature have been demonstrated recently (4–6). In the short-term, GnRH agonist therapy aims at helping the patient to cope with precocious physical development by arrest or regression of the development of sex characteristics and prevention of the early occurrence of menarche or recurrence of menses in girls.

The psychological aspects of CPP have been scarcely studied. In adolescents with a past history of precocious puberty, Ehrhardt et al. found a non-problematic functioning, except for the earlier occurrence of psychosexual milestones, autonomy conflicts and increased psychosomatic complaints (7). In another retrospective study, no negative influence of precocious puberty on well-being in later life could be established (8). Some authors reported that the early occurrence of puberty could be associated with an increased risk of deviant behavior in adolescence and adulthood (9–11). These studies, however, were focused on early physiological variants of puberty, a situation different from actual sexual precocity as seen in our patients. The emotional impact of precocious puberty has been described in only two previous cross-sectional studies (12, 13).

The aim of this longitudinal study was to evaluate the behavioral and affective characteristics in girls with precocious puberty who were treated or followed without treatment during a 2-y period. We also attempted to correlate the changes in psychosocial characteristics with the changes in growth and pubertal development.

Patients and methods

PATIENTS

Among the patients with CPP seen in the pediatric departments of 5 Belgian centers, 20 girls were selected for this study based on the following criteria: (1) central precocious puberty confirmed by a pubertal pattern of gonadotrophin response to GnRH; (2) chronological age at onset of breast development between 5 and 8 y; and (3) informed consent of the patients and the parents for enrolment in this study. The age limits were chosen in order to allow the use of uniform methods for psychological evaluation. Adopted patients were excluded since particular psychological aspects might be involved. In 15 patients, precocious puberty was considered to be idiopathic based on the absence of any relevant history or physical evidence of underlying etiological disorder and negative CT-scan or MRI of the hypothalamo-pituitary region. In five patients, organic etiologies were shown (1 astrocytoma, 1 arachnoidal cyst, 1 pineal cyst and 2 hydrocephalus) and the underlying disease was cured or no longer progressing at the time of this study. Mean chronological age at initial evaluation was 8.2 y (range: 6.6–10.4 y).

Fifteen patients were treated using a slow release formulation of triptorelin (Decapeptyl-Retard®, Ipsen- Biotech, Paris) given as an i.m. injection of 3.75 mg every 4 weeks. Five patients were not treated. Since a randomized distribution of the population into two equivalent groups of treated and untreated patients appeared unethical, the decision of treatment was made by the pediatric endocrinologist in consultation with each individual family, independent of the psychologists. That decision took into account factors such as age, rapidity of pubertal development and bone age advancement, as well as apparent embarrassment of the patients and the parents. This process resulted in a biased selection of 15 treated and of 5 untreated girls. We elected to present the data obtained in the untreated girls, but not to perform any comparison with the treated group.

METHODS

CLINICAL EVALUATION

Pubertal development was estimated according to Tanner using the stages of breast and pubic hair development (14). Height was measured using a Harpenden or wall-mounted stadiometer. These data were obtained at 3-month intervals during a period of 24 months and height velocity was calculated. In 17 patients, we could retrospectively obtain height and weight data measured 2.7 ± 0.5 y (mean \pm SD, range: 1.5–3.8 y) before the diagnosis of precocious puberty. Standard deviation scores (SDS) were calculated with reference to Tanner et al. (15). Weight was measured and calculated as a percentage of ideal body weight for height. Bone age was rated according to Tanner et al. (TW2-RUS) by a single pediatric radiologist (16).

PSYCHOLOGICAL EVALUATION

Semi-structured interviews were developed in order to determine the specific behavioral and affective characteristics in children with precocious puberty and to evaluate the parent's and pediatrician's perception. The design of the interview was based on the systemic theory and family therapy (17). The evaluation involved interviews with the patient and her parents, as well as with the patient alone and with each of the seven pediatric endocrinologists taking care of the families. Standardized questionnaires were also used to evaluate the behavior, the intellectual skills and the global psychosocial functioning. The Child Behavior Checklist (CBC) has been developed by Achenbach et al. as a standardized measure of academic, social competence and behavioral problems in children aged 2–18. French and Dutch translated and adapted versions were used (18, 19). The CBC was filled in by the parents at 1 and 24 months. The Self-esteem Inventory (SEI) was also used (20). This questionnaire was filled in by the patients at 16 and 24 months of study, since it can only be used from the age of 8 y onwards. The intellectual abilities were assessed by the age-appropriate Wechsler scales (21). Other screening instruments were used in order to evaluate the psychological functioning of the child: the observation of play including the use of anatomical dolls (22) and drawing. The psychological evaluation took place 1 month after completion of the diagnostic procedure and initiation of the medical follow-up. The semi-structured interviews and the patient observation sessions took place at 1, 8, 16 and 24 months of study. Two psychologists

(DXH and KL), one French- and one Dutch-speaking, performed the study in order to have the families interviewed in their mother tongue.

The psychological study aimed at evaluating the impact of precocious puberty on the psychosocial functioning of the child. Therefore the data from interviews, standardized questionnaires and observation were integrated. This descriptive, non-randomized study consisted of an in-depth investigation of a limited number of patients. No control group of normal prepubertal girls was studied since we thought it was difficult to motivate families who are not confronted with precocious puberty to commit to regular psychological evaluation and medical visits during a 2-y period.

STATISTICAL ANALYSIS

For CBC and SEI, the individual scores were transformed into Z-scores (SDS), using the reference data of Verhulst and colleagues (19) and Coopersmith (20), respectively. According to the reference data for those questionnaires, the individual scores $> +1$ SD or < -1 SD were considered to be problematic. For the WISC, the age and sex appropriate standards were used as provided by the respective Dutch- and French manuals, as well as the tables for significant difference ($p < 0.05$, student's *t*-test) between the verbal and the performance IQ (21). The significance of differences in behavioral and affective characteristics in relation to some aspects of growth and pubertal development was calculated using comparison of proportions between patient groups and the hypothesis test (23). The growth data are given as mean \pm SD. The significance of changes in mean height and weight was calculated using the paired student's *t*-test (23). The difference was significant at a level of $p < 0.05$.

Results

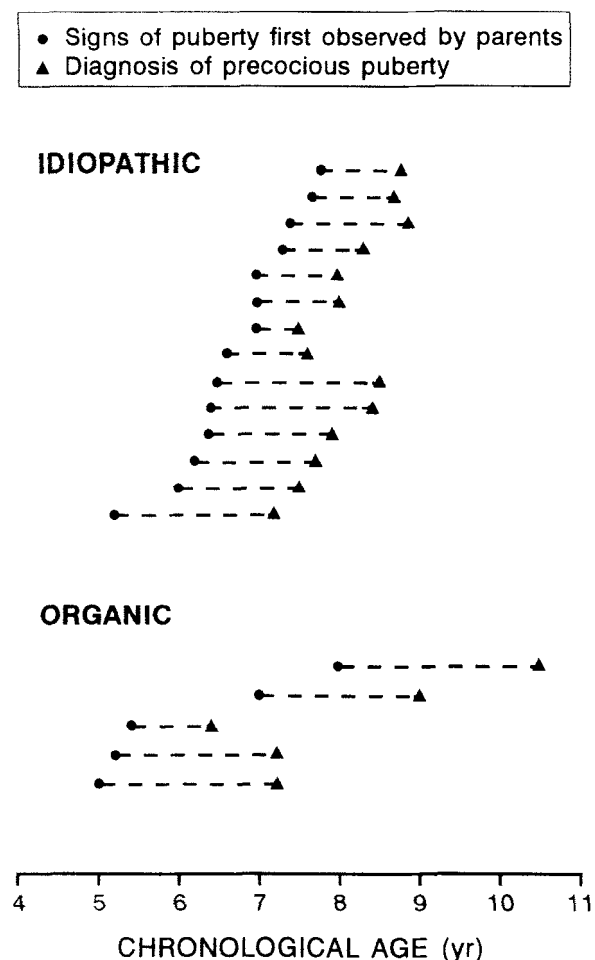
GROWTH AND PUBERTAL DEVELOPMENT

At initiation of the study, mean chronological age was 8.2 y (range: 6.6–10.4) and mean bone age 10.7 y (7.4–12.7). Height velocity was 9.2cm/y (6.4–12.7) which is $+4.4$ SD (1.2–7.8) for chronological age. As shown in **Fig. 1**, there was a mean delay of 1.5 y (range: 0.5–2.2 y) between the time when signs of puberty were first noticed by the parents and the first consultation of a pediatric endocrinologist. The mean delay before consulting was unexpectedly longer ($p < 0.05$) in patients starting puberty before 6.5 y than in those entering puberty after 6.5 y of age (1.8 vs 1.2 y of delay, respectively, $n = 10$ in each group). A long delay before consulting is also seen in the five patients with organic CPP (1.8 y vs 1.4 y in idiopathic CPP, $p < 0.05$) despite ongoing medical care for the primary disease.

As shown in **Fig. 2**, the majority of girls had attained stage M3 of breast development at the start of the study. After 2 y of treatment, 5/15 treated patients showed no or minimal (M1 or M2) breast development. In the other 10 patients treated using long-acting triptorelin, breast development

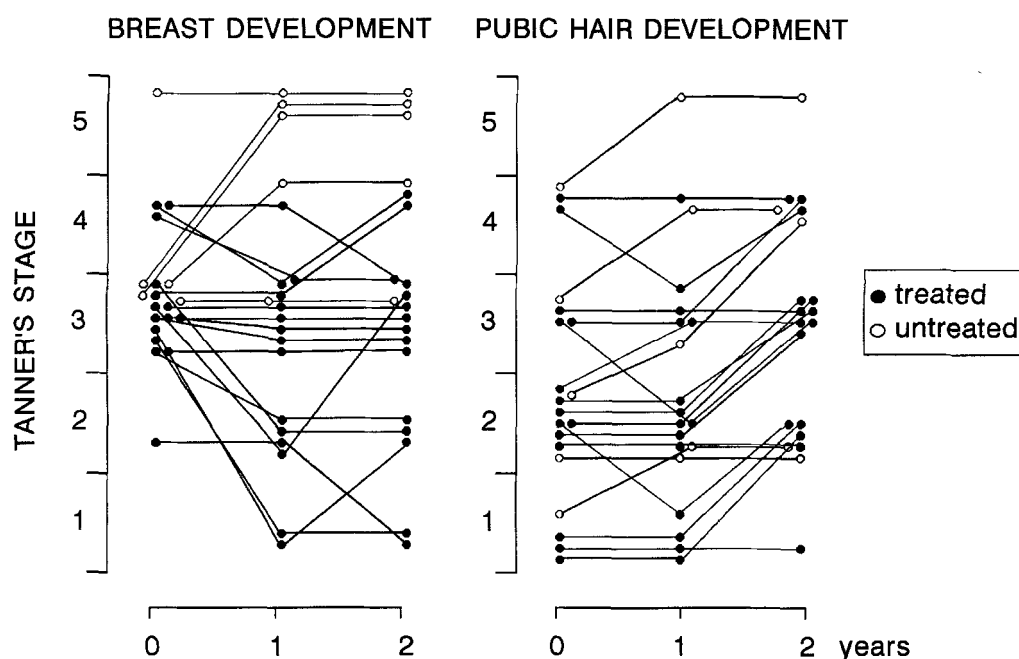
showed either arrest of development ($n = 5$), or transient or partial regression ($n = 5$), although significant breast development ($\geq M3$) persisted after 24 months. In the five untreated girls, progression of breast development to stage M4 or M5 was seen throughout the study, except in one girl who showed unchanged M3 stage. In the majority of patients, pubic hair was absent or incipient (P1 or P2) at the start of the study (Fig. 2). After 2 y, 13/20 patients had attained stage P3-P5, irrespective of treatment. In three girls, menarche occurred 3–7 months before the initial visit.

Fig. 1. Age of 20 girls with idiopathic ($n = 15$) or organic ($n = 5$) central precocious puberty when signs of puberty were first observed by the parents and when diagnosis of precocious puberty was confirmed by the pediatric endocrinologist. The dashed lines indicate the time interval between the two observations.



As shown in Fig. 3, an elevated number of patients had tall stature for chronological age. At diagnosis, mean height SDS was $+1.9 \pm 0.7$ while it was $+0.6 \pm 0.8$ SD, 2.7 y earlier ($p < 0.05$). Although height SDS tended to decrease during the study, nine patients were still above the $+1.8$ SD limit after 2y. The mean weight observed 2.7 y before diagnosis was normal ($102 \pm 8\%$ of ideal body weight). At diagnosis, weight had increased to $113 \pm 15\%$ ($p < 0.05$) and a significant weight excess (weight $> 115\%$ of ideal body weight) was seen in nine patients. During the study, further increase in weight excess was observed in five girls while the others showed no change or even a decrease in weight relative to height. The mean values did not change significantly.

Fig. 2. Changes in Tanner stage for breast and pubic hair development during 2 y of follow-up in 20 girls with central precocious puberty treated using long-acting triptorelin ($n=15$) or untreated ($n=5$).



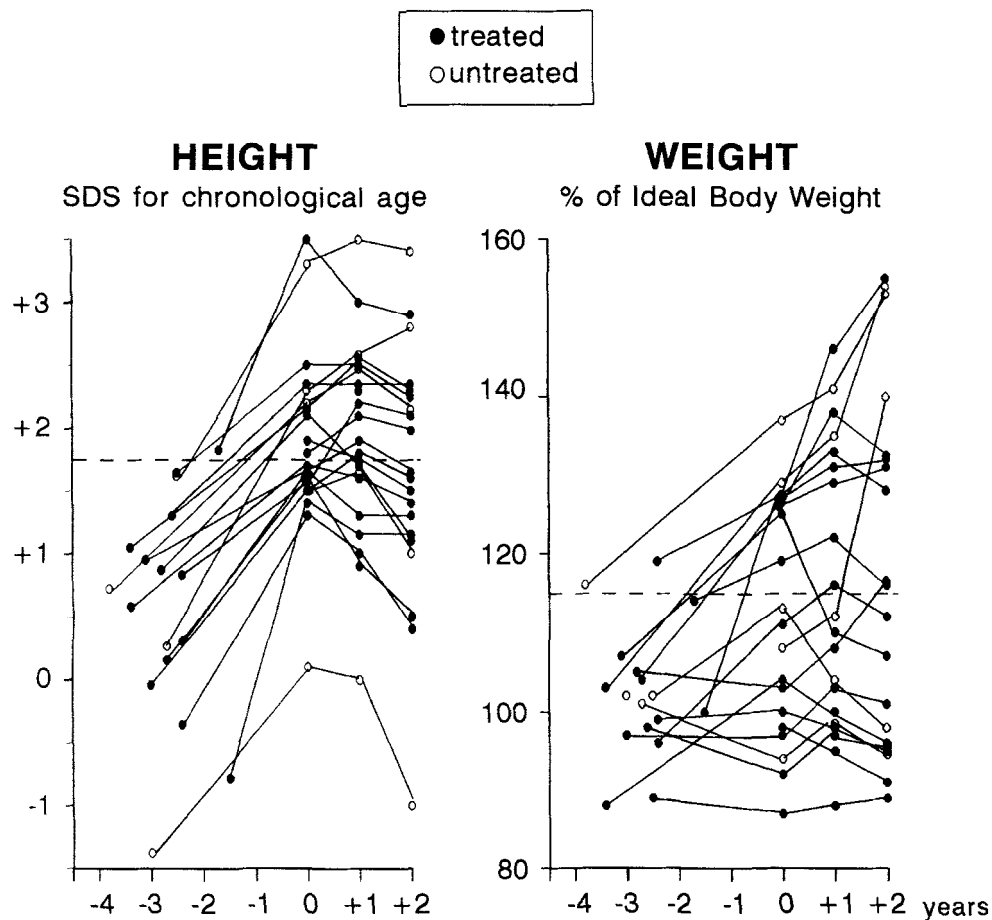
INTELLECTUAL, BEHAVIORAL AND AFFECTIVE CHARACTERISTICS

Normal IQ scores (≥ 90) were obtained in the vast majority of patients (85%). The mean total IQ was 102 (range: 64–129). While the verbal IQ appeared to be normally distributed, the performance IQ was negatively skewed (coefficient of skewness: -0.6) and significantly lower than the verbal IQ in six girls ($p < 0.05$). The total IQ scores were consistent with the school situation, 18/20 girls attending an appropriate grade for their age. One patient was retarded at school and one attended special elementary school. In none of the patients, earlier school enrolment or school acceleration had been considered. In 3/20 patients, transient decline in school performance associated with the emotional upheaval resulting from precocious puberty was reported by the parents.

Differences in concern about precocious puberty between the patients, the parents and the pediatric endocrinologists appeared from the semi-structured interviews (Fig. 4). Initially, all the girls expressed fear of peer comments about physical differences. The chief-complaint was breast development while pubic hair development and tallness appeared to be less problematic. Some patients (7/20), including 1/3 girls who had menarche before being referred, felt concerned about the possible occurrence of menarche. Only one patient worried about possible short adult stature though information on this issue was provided to all of them by the pediatric endocrinologists. The patient's preoccupation with physical differences did not appear as obvious for some of the mothers, fathers and pediatric endocrinologists. The possible occurrence of menstruation was an important matter of concern for the mothers in contrast to the fathers. Despite extensive information on the risk of short adult stature which is the leading concern of the pediatric endocrinologists, only one-third of the parents brought up that issue during the interviews. After 2 y, the evidence of concerns was less obvious among the parents and pediatric endocrinologists

while 13/20 girls still worried about physical differences from peers. Also, some patients began worrying about adult stature.

Fig. 3. Changes in height (SDS for chronological age) and weight (% of ideal body weight) measured 2.7 y (range: 1.5–3.8 y) before the diagnosis of precocious puberty and after 2 y in 20 girls with central precocious puberty treated using long-acting triptorelin ($n = 15$) or untreated ($n = 5$). The dotted lines indicate the arbitrary limits between normal and tall stature (+1.8 SD equivalent to 90th centile) and between normal weight and obesity (weight $\geq 115\%$ of ideal body weight).



Some particular behavioral and affective characteristics have been observed in girls with precocious puberty. The most striking feature was embarrassment about pubertal development in all 20 girls. In several girls, this embarrassment was reinforced by comments from adults and mockeries or even attacks from peers (e.g. pinching breasts). After 2 y (**Fig. 5**), embarrassment about pubertal development had disappeared in 6/15 treated girls, five of them showing marked regression of breast development ($\leq M2$). These changes occurred irrespective of progression of pubic hair, weight and height.

Initially, fear of sexuality was observed in 17/20 patients including 12 girls from the treated group. After 2y, this feeling remained present in a majority of them (**Fig. 5**). Half of the parents associated the early physical development of their daughter with questions about precocious sexuality. The

risk of sexual abuse has been brought up by the parents of 3/20 girls. In 6/20 families, the psychological evaluation revealed a problematic family functioning (withdrawn families, with confusion among the generations). However, no situation of sexual abuse was evident in any of the studied families.

Fig. 4. Number of patients, mothers, fathers and pediatric endocrinologists who appeared to be concerned about physical differences from peers, occurrence of menarche and short adult stature at start of the study (1 month after initiation of medical management) and after 2 y.

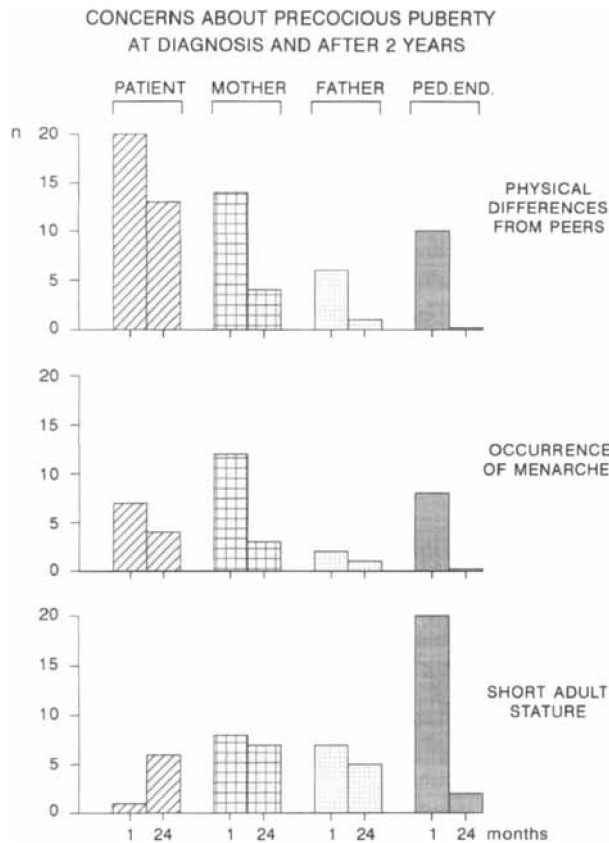
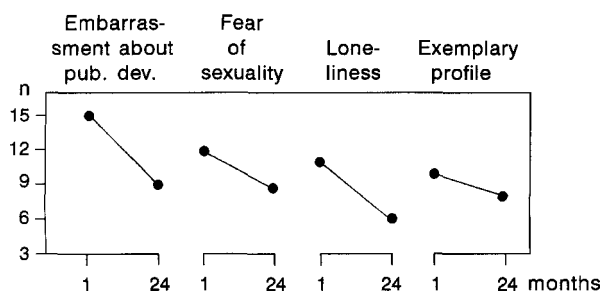


Fig. 5. Changes in some behavioral and affective characteristics in 15 girls with central precocious puberty at 1 and 24 months of study during therapy using long-acting triptorelin.



Feelings of loneliness and complaints about having no or few friends were expressed initially by 14 girls. The girls were often described as solitary by their parents. This problematic social functioning

was confirmed by elevated withdrawal scores ($> +1$ SD) at the CBC in seven girls (**Fig. 6**). The majority of patients (14/20) initially appeared as exemplary girls who were described as discreet, reserved or model. Beyond the exemplary appearance of the patients, the parents reported intense emotional reactions in half of them. These reactions involved easy crying ($n = 10$), shyness ($n = 11$) and sticking to the parents ($n = 10$). The emotional lability was confirmed by elevated anxiety and depression scores ($> +1$ SD) at CBC in eight girls (**Fig. 6**). Opposite emotional reactions such as aggressiveness were reported by the parents of eight girls. After 2 y, a reduced number of treated girls showed an exemplary profile and suffered from loneliness (**Fig. 5**). These characteristics were seen in all five untreated girls after 2 y of study.

At 24 months, the total self-esteem score (SEI) *appeared* to be positive in all 20 patients, 8 of them showing scores $\geq +1$ SD. The mean general and social self-esteem scores were not elevated ($+0.39$ and $+0.32$ SD, respectively). In contrast, the mean scores obtained at family and school scales were elevated ($+0.83$ and $+1.49$ SD, respectively) and a majority of individual values were $> +1$ SD. These data are consistent with the exemplary profile observed in many of the patients. It is noteworthy that a social desirability score > 1 SD was obtained in 7/20 patients indicating that the self-esteem scores may have been biased by the wish of some patients to present themselves as nicer and better than they really felt.

Precocious pubertal development was associated with various somatic complaints. Weight excess was a matter of concern in eight girls; eight reported stomachaches and four headaches without any underlying cause shown at radiological or endoscopic examinations. In six girls, elevated somatic complaint scores at the CBC confirmed those findings (**Fig. 6**). During the study, the scores of withdrawal, anxiety/depression and somatic complaints increased in some patients while they decreased in others, irrespective of treatment (**Fig. 6**).

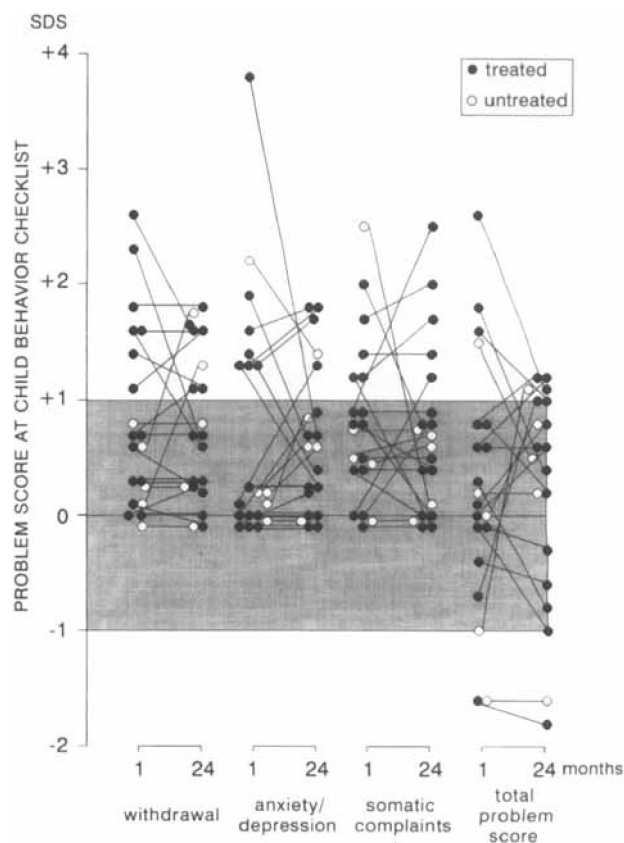
Discussion

In this study, a particular affective and behavioral pattern is described in girls with precocious puberty. They present themselves as exemplary and model. Beyond this appearance, however, intense emotional reactions are reported by parents and observed during psychological evaluation. We cannot establish any linear causality between the observed pattern and precocious puberty. Repeated patient observations have, however, triggered some hypotheses about the impact of precocious puberty on psychological functioning.

The relatively long delay of 1.5 y between the onset of puberty and the first consultation can be due to a cultural taboo on sexuality and pubertal development. An even longer delay of 3.0 ± 1.5 y has been reported in a large North American study suggesting the broad prevalence of that issue (5). From the parent's interviews, defensive reactions such as denial, rationalization and minimization of precocious puberty before consultation, have appeared retrospectively. We hypothesize that such a defensive attitude could be reinforced by the exemplary and apparently non-problematic behavior of most patients, thus accounting for delayed consultation. With time,

these defensive reactions might have been overcome by the progression of pubertal signs and the fear of possible menarche.

Fig. 6. Changes in problem scores at the Child Behavior Checklist filled in by the parents of 20 girls with central precocious puberty at 1 and 24 months of the study. The data from three subscales (withdrawal, anxiety/depression, somatic complaints) and total problem score are shown. The shaded area represents the normal range.



With respect to intellectual functioning, normal mean IQ scores were found in this study, which agrees with the data reported by other authors (24–26). Interestingly, the performance IQ is significantly lower than the verbal IQ in several girls. Galatzer et al. have reported that the mean verbal IQ score is higher in precocious puberty patients than in controls as a possible result of sex hormone influence on brain development (24). Meyer-Bahlburg et al. have found performance IQs lower in precocious puberty patients than in controls (25). These authors think that early maturation can be associated with lower spatial development due to weakness of the right hemisphere functioning. In our study, as well as that of Solyom et al. (12), academic performance does not appear to be affected by precocious puberty. An important school investment may be related to the exemplary behavior of the patients, in an attempt to compensate for the physical differences. In contrast to other studies (27), no school grade skipping or earlier school enrollment was observed in our patients.

The semi-structured interviews showed that in all girls with precocious puberty, the physical changes are the chief-preoccupation, particularly breast development. The parents and the physicians were mainly concerned about the future risks such as menarche and short stature. These risks do not appear as important in the girls, possibly because of a limited capacity of projection into the future. Embarrassment about breast development in girls with precocious puberty has been mentioned in a previous study of a small group of patients (12). Other authors have stressed a strong sense of being different (13). Despite a therapeutically induced arrest of pubertal development, the vast majority of the patients remain concerned about physical differences from peers, mainly breast development, after 2 y. Long-acting triptorelin therapy results in disappearance of that concern only in the five girls who showed regression of breast to minimal or absent development. Such an observation may urge the physician to begin early treatment of precocious puberty. This, however, may not be possible because of the long interval before consultation about precocious pubertal development. In addition, early treatment might not be desirable in some variants of precocious puberty with very slow progression or spontaneous arrest who should not require any treatment (6). While the regression of breast development has a positive effect on embarrassment, pubic hair has no direct impact on the affective and behavioral pattern. A possible explanation is that this pubertal characteristic can easily be hidden from peers.

Social functioning is markedly affected by precocious puberty. Jackson et al. (13) have reported low popularity scores revealing difficulties in peer relationships. In a study by Sonis et al. (28), a withdrawn score > 2 SD at CBC has been reported in as many as 45% of patients with precocious puberty. We can confirm this finding, although it appears to be less dramatic in our study than it does in the study of Galatzer et al. (29). Adolescents with a history of precocious puberty remember withdrawal behavior during elementary school (8). Social withdrawal appears to result from the uneasiness related to the physical differences from peers as well as from the impossibility of sharing those concerns with peers. Therefore, some girls tend to seek out older peers, as also mentioned by Solyom (12) and/or take refuge into the family. When a closed family functioning is present, this can create conditions propitious for sexual abuse, a risk previously emphasized by Herman-Giddens et al. (30). Although concomitant incest and precocious puberty have not been reported so far, we could identify some families at increased risk of sexual abuse. These families warrant specific preventive management.

In girls with precocious puberty, the observed exemplary profile could be interpreted as a way of coping with their early mature appearance. Also, the exemplary behavior might be a defensive attitude since being unnoticed could reduce their feeling of physical discomfort. After 2 y, an exemplary profile is still observed in many patients. Some girls present themselves as more exemplary and they appear more lonely with more problematic scores at CBC than at the start of the study. Such a finding can be interpreted as a consequence of isolation by the progression of pubertal development and the increasing differences from peers. Due to the small number of patients, however, these data have to be considered with caution. When the 5 treated patients with breast regression to minimal development are compared with the 10 other treated patients, no differences are observed with respect to loneliness, exemplary behavior and fear of sexuality, which all show some decrease after 2 y. All of the treated girls appear to have fewer difficulties in

coping with precocious puberty. This might result from the relief and support provided by treatment irrespective of the physical effects as well as the attention paid to the girls and the parents during the study.

Though the exemplary behavior is clearly put forward by the girls with precocious puberty, an intense emotional lability is observed. Emotional reactions have been described by others: aggressiveness or depression (28), anxiety, shyness and insecurity (13). Solyom also reports excessive shyness that he interprets as a defensive measure against phase-appropriate exhibitionistic feelings (12). We integrate shyness into the profile of exemplary behavior. These characteristics of girls with precocious puberty cannot be extrapolated to those of normal adolescence. Adolescent girls predominantly show emotional reactions.

The somatic reactions (weight gain) and the somatic complaints cannot be related to the organic or idiopathic etiology of CPP. The high prevalence of somatic complaints has also been pointed out by Sonis et al. (28). Adolescents with a history of precocious puberty report considerably increased psychosomatic symptoms which are interpreted as a result of increased sensitivity to hormonal fluctuations throughout the menstrual cycle (7). Weight excess has been commonly reported in girls with precocious puberty. It appears to be part of several somatic complaints and can be integrated into the physical reactions to the emotional upheaval caused by precocious puberty. This study shows that weight excess usually develops before diagnosis while few changes are observed during follow-up and therapy.

The observed behavioral and affective pattern in girls with precocious puberty does not strikingly change during the 2-y follow up. Since these girls have not yet become adolescent after those 2 y, a further longitudinal study of our patients up to the age of adolescence seems very important to assess whether this profile is still or no longer present at that period. In addition, different authors have shown increased behavioral risk and deviance in adolescents with early onset of puberty, a condition which is, however, different from sexual precocity (9–11). The discrepancy between these studies and others concluding minor long-term effects of sexual precocity (7, 8), may be related to differences in therapeutic support and management provided to the patients. Such a hypothesis emphasizes the need for further studies comparing treated and untreated patients in the long-term.

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References

1. Comité F, Cutler GB, Rivier J, Vale WW, Loriaux DL, Crowley WF. Short-term treatment of idiopathic precocious puberty with a long-acting analogue of Luteinizing-Hormone Releasing Hormone. *N Engl J Med* 1981; 305: 1546–50.
2. Boepple PA, Mansfield MJ, Wierman ME, Rudlin CR, Bode HH, Crigler JF, Crawford JD, Crowley WF. Use of a potent, long acting agonist of Gonadotropin-Releasing Hormone in the treatment of precocious puberty. *Endocr Rev* 1986; 7: 24–33.
3. Heinrichs C, Craen M, Vanderschueren-Lodeweyckx M, Malvaux P, Fawe L, Bourguignon IP. Variations in pituitary-gonadal suppression during intranasal buserelin and intramuscular depot-triptorelin therapy for central precocious puberty. *Acta Paediatr* 1994; 83: 627–33.
4. Kauli R, Kornreich L, Laron Z. Pubertal development, growth and final height in girls with sexual precocity after therapy with the GnRH analogue D-Trp⁶-LHRH. *Horm Res* 1990; 33: 11–7.
5. Oerter KE, Manasco P, Bames KM, Jones J, Hill S, Cutler GB. Adult height in precocious puberty after long-term treatment with deslorelin. *J Clin Endocrinol Metab* 1991; 73: 1235–40.
6. Brauner R, Adan L, Malandry F, Zantleifer D. Adult height in girls with idiopathic true precocious puberty. *J Clin Endocrinol Metab* 1994; 79: 415–20.
7. Ehrhardt AA, Meyer-Bahlburg HFL. Idiopathic precocious puberty in girls: long-term effects on adolescent behavior. *Acta Endocrinol* 1986; 279 Suppl: 247–53.
8. Schoevaart CE, Drop SLS, Otten BJ, Slijper FME, Degenhart HJ. Growth analysis up to final height and psychosocial adjustment of treated and untreated patients with precocious puberty. *Horm Res* 1990; 34: 197–203.
9. Duncan P, Ritter P, Dombusch S, et al. The effects of pubertal timing on body image, school behavior and deviance. *J Youth Adolesc* 1985; 14: 227–35.
10. Magnusson D, Stattin H, Allen V. Biological maturation and social development: a longitudinal study of some adjustment processes from mid-adolescence to adulthood. *J Youth Adolesc* 1985; 14: 167–84.
11. Orr DP, Ingersoll GM. The contribution of level of cognitive complexity and pubertal timing to behavioral risk in young adolescents. *Pediatrics* 1995; 95: 528–33.
12. Solyom AE, Austad CC, Sherick I, Bacon GE. Precocious sexual development in girls: the emotional impact on the child and her parents. *J Pediatr Psychology* 1980; 5: 385–93.
13. Jackson PL, Ott MJ. Perceived self-esteem among children diagnosed with precocious puberty. *J Pediatr Nursing* 1990; 5: 190–203.
14. Tanner JM. *Growth at adolescence*. 2nd ed. Oxford: Blackwell, 1962.
15. Tanner JM, Whitehouse RH, Takaishi M. Standards from birth to maturity for height, weight, height velocity and weight velocity: British children, 1965. *Arch Dis Child* 1966; 41: 454–71.
16. Tanner JM, Whitehouse RH, Cameron N, Marshall WA, Healy MJR, Goldstein H. *Assessment of skeletal maturity and prediction of adult height (TW2 method)*. 2nd ed. Academic Press: London, 1983.
17. Ausloos G. *Systèmes-Homéostasie-Equilibration, Thérapie familiale*. Genève 1981; 2: 187–203.

18. Achenbach T, Edelbrock CM. Manual for the Child Behavior Checklist and Revised Child Behavior Profile. Burlington, Vermont: Queen City Printers, 1983 (Adaptation Française, E Fombonne. Département de Recherche C.A.B., Paris, 1986).
19. Verhulst FC, Koot JM, Akkerhuis GM, Verman JW. Praktische Handleiding voorde CBCL (Child Behavior Checklist). Assen: Van Gorcum, 1990.
20. Coopersmith S. Self Esteem Inventory. Palo Alto: Consulting Psychologists Press, Inc., 1981 (Adaptation française, by Les Editions du Centre de Psychologie Appliquée, Paris, 1984).
21. Wechsler D. Manual for the Wechsler Intelligence Scale for Children-Revised. New York: The Psychological Corporation, 1974 (Traduction et adaptation par les éditions du Centre de Psychologie Appliquée, 1981. Lisse: Nederlandse Bewerking, Swets & Zeitlinger BV, 1986).
22. Goldberg CC, Yates A. The use of anatomically correct dolls in the evaluation of sexually abused children. *Am J Dis Child* 1990; 144: 1334–6.
23. Altman DG. Practical statistics for medical research. 1st ed. Padstow: TJ Press Ltd, 1991.
24. Galatzer A, Beth-Halachmi N, Kauli R, Laron Z. Intellectual function of girls with precocious puberty. *Pediatrics* 1984; 74: 246–9.
25. Meyer-Bahlburg HFL, Bruder GE, Feldman JF, Ehrhardt AA, Healey JM. Cognitive abilities and hemispheric lateralization in females following idiopathic precocious puberty. *Devel Psychol* 1985; 21: 878–87.
26. Mouridsen SE, Larsen FW. Psychological aspects of precocious puberty. An overview. *Acta Paedopsychiatrica* 1992; 55: 45–9.
27. Ehrhardt AA, Meyer-Bahlburg HFL. Psychosocial aspects of precocious puberty. *Horm Res* 1994; 41 Suppl 2: 20–35.
28. Sonis WA, Comité F, Blue J, Pescovitz OH, Rahn CW, Hench KD, Cutler GB, Loriaux LD, Klein RP. Behavior problems and social competence in girls with true precocious puberty. *J Pediatr* 1985; 106: 156–60.
29. Galatzer A, Laron Z. Behavior in girls with true precocious puberty. *J Pediatr* 1985; 108: 790–1.
30. Herman-Giddens ME, Sandler AD, Friedman NE. Sexual precocity in girls. An association with sexual abuse? *Am J Dis Child* 1988; 142: 431–3.