

The Peutz Jeghers Syndrome: A Case Report

Ali El Mahdi Haddam¹, Soumeya Fedala²

¹Department Of Endocrinology Bologhine Hospital

²Department Of Endocrinology Bab El Oued Hospital 16000

Summary: Peutz - Jeghers syndrome (PJS) is an autosomal dominant disease that combines hamartomatous polyposis ,a peri- orificial lentiginose and a high risk of associated cancers. We report the observation of a girl 07 years old of personal history of acute intestinal intussusception occurred a year ago who consults for signs of early puberty and the onset of vaginal bleeding up to 06 months . The child has a sexual stage development S3P3R (+) , an advance of height (11 years) and bone age (12years) and the presence of brownish macules on the buccal mucosa . During her hospitalization, she developed severe abdominal pain predominant in the right iliac region , with vomiting and a stop materials and gas. The diagnosis of acute intussusception was made and surgical resection of the small intestine is rapidly performed. Histological examination showed a hamartomatous polyp with moderate dysplasia. Endocrine exploration concluded the diagnosis of pseudo- precocious iso sexual puberty related bilateral tumor of the granulosa and digestive endoscopy showed the presence of multiple polyps stepped located at the fundus and small intestine. The girl was treated with cyproterone acetate (for lack of aromatase inhibitors) and directed to a surgical bilateral oophorectomy because of the high risk of neoplasia. The SPJ can affect many organs with an increased risk of cancers. Obstructive episodes are the main clinical manifestations. We must recognize the syndrome especially if it associate with precocious puberty and / or peri orificial lentiginose

Keywords: Peutz jeghers; polyps ;peri oral lentiginose; hamartoma ;neoplasia

I. Introduction

Peutz - Jeghers polyposis is a hamartomatous of the whole digestive tract, which is accompanied by a labile lentiginose of oral mucosa, the anal area and the fingers. This is a rare autosomal dominant inheritance linked to the mutation of STK11 gene (19 p13.3) and associated with an increased risk of cancer (estimated at 93 % cumulative risk) (Tovar J.A. et al ,1983). The organs most commonly affected are the gastrointestinal tract (esophagus, stomach, small intestine, colon, rectum and pancreas), lung, prostate, breast, and reproductive organs. The mucocutaneous hyperpigmentation is the revealing sign of the disease. Gastrointestinal polyps the second hallmark of the disease, can occur immediately by digestive complications. Sometimes the syndrome may be revealed by signs of precocious puberty (Bourauoi S. et al,2008). We report a case in this regard.

Clinical observation:

AS aged 7 years was admitted in the service for exploration of early puberty. It has no history of disease with the exception of two episodes of intussusceptions treated which has not been the subject of prior exploration.

The child had since the age of five years the development of secondary sexual characteristics with bilateral breast and pubic hair thrust. It was only before the onset three months earlier menstrual cycles accompanied by abdominal pain that the child is taken in endocrinology consultation.

Clinical examination revealed a patient in good condition with pubertal development stage S4 P3 tanner (fig 1), an acceleration of the rate of linear growth with a size of 1.43 cm (4 DS / M, Sempé and pyle), a weight of 33kg (> P97 +) and an advance of bone age, estimated at 12 years (Greulich and Pyle atlas).

We also noticed the presence of perioral and buccal mucosa brownish macules (fig 2) appeared at the age of two years which haven't worried parents as the mother had the same rash. The remainder of the physical examination was unremarkable. Hormonal exploration was in favor of early peripheral puberty (Table I) and abdominopelvic magnetic resonance imaging revealed the presence of two bilateral heterogenous ovarian masses having a malignant look with an intensely irregular contour after contrast enhancing and measuring 4 cm. The uterus was pubescent guy with visualization of a line of emptiness and increased ovarian size (Fig. 3).

The tumor markers were with no abnormalities (Table I). The coexistence of cutaneous and mucosal hyperpigmentation and history of invagination has directed us to the evocation of SPJ. Digestive exploration (intestinal endoscopy, colonoscopy and upper gastrointestinal endoscopy) was undertaken highlighting many polyps of variable size scattered at the stomach, duodenum and jejunum. The rest of the para-clinical exploration showed no other extra intestinal neoplasm. The genetic study was not performed.

Bilateral oophorectomy is undertaken as well as the removal of larger polyps. Histopathological study was in favor of malignant granulosa cell tumors and hamartomatous polyps features of SPJ with no signs of degeneration. The patient is put under suppression puberty therapy with rigorous clinical and laboratory monitoring. Four years after surgery, the clinical picture was stationary.

Table I: hormonal results

Parameter	results
FSH mui/ml (N : 0,2-10)	0,56
LH mu/ml (N :0,2-8)	0,27
E2 nmol/l(Before puberty< 0,11)	10
BHCG mu/ml (N<35)	0
urinary Alpha fetoprotein /ml (N<10)	0,56
CA 19/9 ui/ml (N<40)	5,88
Ca1 25 ui/ml (N<35)	8,45

II. Discussion

Peutz-Jeghers -Touraine syndrome (SPJ) is a rare condition(1 /200 000 births). It is defined by at least 3 Peutz-Jeghers hamartomatous polyps histologically confirmed and the association of peri- orificial lentiginose and family history of polyps (Tovar J.A.et al ,1983) . There is no predominance of sex ,racial or ethnic recognized factor. The syndrome usually occurs in adolescence with a mean age at diagnosis of 23 years for men and 26 years for women (McGarrity T.J. and Amos C. ,2006). The first description was in 1921 when Jan Peutz, reports the case of a family with gastrointestinal polyposis and mucocutaneous lentiginose (Heymann W.R.,2007) (Tovar J.A .,1983). The SPJ is an autosomal dominant disorder with a high penetrance (more 90 %) and a variable expression . It is linked to an inactivating mutation of a tumor suppressor gene. Currently, at least two different genes can be alternately engaged. The STK11 gene (19 p13.3), recently identified, is responsible for the disease in 70% of families (Mehenni H . et al,1998). It encodes a protein family of serine-threonine kinase, and a biallelic inactivation in hamartomatous lesions evokes its tumor suppressor role, a new mechanism for a gene with a kinase domain mutations. The mutations are located on the entire coding sequence, and the knowledge of the spectrum of constitutional mutations doesn't define correlations between their nature or their position and pathological consequences (Nakagawa H. et al, 1998). It is nevertheless possible to propose, on the basis of a genetic test diagnostic, a specific monitoring to people carrying the familial mutation (Nakagawa H. et al, 1998) (Rautou P.E., et al, 2007).

Digestive polyposis is the main clinical manifestation (McGarrity T.J. and Amos C., 2006). In over half of cases, it is revealed by acute invagination or a mesentery strangulation, intestinal necrosis and perforation. Chronic and recurrent abdominal pain may be observed, more rarely gastrointestinal bleeding responsible for chronic anemia or delivery of a polyp through the anus (Schreibman I.R. , 2005). Polyposis occurs in half of the cases before 20 years and affects the entire digestive tract: 90% small intestine (jejunum + + + +) stomach 24% colon 9%. In a third of cases, it appears before 10 years. There is no relationship between the size of polyps and degeneration potential. It is estimated that 2/75 may degenerate (Cherki S., Adham M. and Bizollon T.,2002). The mucocutaneous lentiginose appears before 2 years. It is located essentially at the lower lip, eyes, nose (66%) , hands and feet (62%), more rarely in the perianal mucosa ((Tovar J.A.et al ,1983) (Heymann W.R.,2007) (Cherki S., et al, 2002) . The evolution is marked by the disappearance of skin lesions in 50% before 20 years while mucosal lesions persist (Tovar J.A.,1983). The lentiginose usually precedes the onset of polyps and their manifestations. It is a clinical marker of the disease and its association with gastrointestinal polyps is highly suggestive (Bouraoui S. et al,2008) (McGarrity T.J. and Amos C.) (Heymann W.R.,2007).

PJ syndrome is often associated with benign or malignant gastrointestinal and extra-intestinal tumors that will be systematically searched. Combined tumor risk is high of about 94%. Women seem most affected (18.5 %) than men (6.2 %) (Higham P., Alawi F., Stoopler E.T., 2010) (von Herbay A., Arens N., Friedl W., 2006) (Conneely J.B., Kell M.R. and Boran S.,2006) . The organs most commonly affected are the gastrointestinal tract (esophagus, stomach, small intestine, colon, rectum and pancreas), lung, prostate, breast, and reproductive organs (von Herbay A., Arens N. and Friedl W., 2005).

Gonadal neoplasias are present in 22 to 48% of cases (von Herbay A., Arens N. and Friedl W., 2005). They are very early onset between four and seven years and are responsible for isosexual or heterosexual pseudo-puberty. These are basically: Sertoli cell Testicular tumors and granulosa ovarian bilateral and small tumors ((Tovar J.A.et al ,1983) (Sohl H.M., Azourv R.S.and Najjar S.S. ,1983) . Besides these neoplasms, other malignant tumors can be developed in adulthood as breast adenocarcinoma, papillary or follicular carcinoma of the thyroid and lung neoplasms (Girdiello F.,1987).

The differential diagnosis of SPJ arises mainly with other hereditary family polyposis as familial adenomatous polyposis, Gardner's syndrome and generalized juvenile polyposis. However, the limited location of polyps and the absence of extra-intestinal signs are in against the diagnosis (Nakagawa H. et al, 1998).

Evolution of patients with this condition is unpredictable. In the short term, risks are associated with acute complications (gastrointestinal hemorrhage, acute invagination). In the medium and long term, the prognosis is reserved. High neoplastic risk is a cause of death before age 30 in particular by colon cancer. Survival at 60 years is difficult to assess. It is significantly reduced compared to the general population but could be improved if strict and rigorous monitoring. Support of SPJ is based primarily on the monitoring and treatment of hamartomatous polyps. The frequency of monitoring of patients with this disease been no consensus, but it is desirable that asymptomatic patients have a high endoscopy every 2 years for the monitoring and removal of polyps. The magnetic resonance imaging showed a success as a method for monitoring the small intestine and testis, abdominal ultrasound is performed for the detection of pancreatic cancer. In the women, mammography, Pap smears and trans-vaginal ultrasound is done every 1 to 2 years. Blood counts should be performed to detect anemia caused by blood loss (Cherki S., et al, 2002) (von Herbay A., Arens N. and Friedl W., 2005) . Secondary occlusive episodes to polyps are self-limiting in children and polypectomy is not systematic. It is important to perform screening and early treatment of polyps and other extra-intestinal tumors. Intestinal resection should be as economical as possible.

III. Conclusion

Peutz-Jeghers-Touraine Syndrome is a rare inherited disorder involving in its complete form gastrointestinal polyposis, mucocutaneous lentiginose and various tumor manifestations. Its natural evolution is still unknown and remains unpredictable to the variability of clinical expression disease. Because of the high neoplastic risk, close monitoring of these patients is necessary to detect precociously associated cancers and treat them. Close collaboration between pediatricians, gastroenterologists, endocrinologists and Gynecologists is essential to reduce this mortality.

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