Incontinentia Pigmenti with Dental Anomalies: A Three-generation Study

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Abstract. Three individuals with incontinentia pigmenti from one family spanning three generations are described. All three had associated dental anomalies. The pattern of inheritance is consistent with the theory of an X-linked gene, dominant in females and lethal in males.

Key words: Incontinentia pigmenti; Dental anomalies

Incontinentia pigmenti (IP) is an uncommon genodermatosis that occurs almost exclusively in female infants.

IP presents distinct clinical manifestations. The disease usually appears at birth, presenting with inflammatory lesions consisting of erythematous macules, papules and bullas arranged in a linear pattern on the extremities and torso. In the typical case this stage is followed by a verrucous stage after 2-6 weeks, lasting for a few months. During the verrucous stage or a few months thereafter the pigmented stage appears, not necessarily on the same places as the inflammatory lesions, with bizarre pigmentations mostly on the torso. These pigmentations gradually fade and are usually absent by adulthood.

In contrast to the benign skin manifestations there are also developmental defects in 80% of patients with IP, the most serious being ocular anomalies leading to blindness (3). Other reported defects are scalp abnormalities, nail dystrophy, dental anomalies and disorders of the central nervous system.

This report describes a family in which members of three successive generations have IP combined with dental anomalies (Fig. 1).

CASE REPORT

The propositus (IV, 1) was born weighing 3.3 kg after an uncomplicated 43-week pregnancy. Two days after delivery a rash was noticed consisting of pronounced erythema, papules and vesicles, having a peculiar band-shaped distribution over the buttocks, dorsally on the thighs, laterally on the abdomen, but sparse on arms and cheeks. Three days later the rash had almost disappeared but after a few days a similar rash appeared, lasting for a few days.

A blood leukocytosis of 22 600 was found, whereof 4060 were eosinophils. A punch biopsy was consistent with the second phase of IP, with dyskeratotic cells in the epidermis.

An examination at the age of 3 months revealed pigmentations medially on the thighs and on the left labium majus. At the age of 18 months there were small pigmented patches laterally on the torso and a larger irregular pigmented patch on the left buttock. Neurological and ophthalmological examinations were normal. Chromosomal analysis showed a normal 46, XX pattern. The child, now 27 months old, has developed normally except that she has no primary laterals in the upper jaw (Fig. 2).

Fig. 1. Pedigree of family. Propositus is indicated by arrow.
Family data

The propositus’ mother (III, 2) also has IP. One day after birth she was examined by a dermatologist and found to have a vesicular, striated rash on chest and hands. This was later followed by a verrucous stage. Today (age 19) the skin changes consist of two irregular pigmentation on her left breast. She has a partial hypodontia with absence of six permanent teeth and pegged malformations (K.-V. Sarnäs, orthodontist, Centre for Cranio-facial Anomalies, General Hospital, Malmö) (Fig. 3). She has had two spontaneous abortions (one female, one sex unknown).

The propositus’ grandmother (II, 2), also has IP. According to the obstetric record she was born with a pustular crusted eruption covering large parts of her body, that healed spontaneously in a few days. There were similar recurrent episodes during her first 9 months of life. Today (age 41) her skin changes consist of atrophic, hairless, hypopigmented streaks laterally on the thighs and a patch of alopecia in the occipital region. She has partial hypodontia with absence of 7 permanent teeth. She has two normal sons and has had three spontaneous abortions (sex unknown).

The propositus’ great-grandmother, now aged 66 (I, 1), has no IP, according to her own history and examination by the author. She has three normal sons and has had four spontaneous abortions (sex unknown).

DISCUSSION

Two theories have been put forward concerning the mode of inheritance in IP. The disease is due either to an autosomal, dominant gene, which is sex-limited in its expression, producing the defect only in females, or is due to a sex-linked gene carried on the X-chromosome, dominant in females and lethal in males (2, 3).

If the theory of an autosomal, dominant gene, sex-limited in its expression, and producing the defect only in females, were the correct one, one would expect a ratio of affected females: normal females: normal males (half of whom would be carriers) of 1:1:2. Carney’s statistical analyses of cases published in the literature (593 females, 16 males) have not been consistent with these ratios (1). Also, there has been no report of inheritance of IP via the father’s mother, which would have proved this theory to be correct.

The theory of a sex-linked gene carried on the X-chromosome, dominant in females and lethal in males would give an expected ratio affected females: normal females: normal males: aborted males of 1:1:1:1. These ratios accord well with Carney’s statistical analyses and with the only report concerning IP in four generations (4). Our pedigree is consistent with this latter theory, since the affected individuals are all females, transmission was by females only, affected relatives were only maternal females and the number of spontaneous abortions was great (Fig. 1).

The dental defects characteristic of IP are partial (occasionally complete) anodontia or pegged (conical) deformity of some of the teeth, or both. The disorders may involve the deciduous or permanent teeth, or both. The frequency of dental defects has probably been underestimated earlier because deciduous teeth do not begin to erupt until several months after birth. In an analysis of patients over one year of age, Carney reported that 64.7 % have some major dental abnormality (1). The most common was hypodontia (43.1%). Delayed tooth eruption was found in 18.0 % of cases. Pegged and otherwise malformed teeth were reported in 30.4 %.

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Usually, incisors and canines were affected. All our 3 patients exhibited dental abnormalities of one or more of the types mentioned above.

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REFERENCES


Forty Years of Diarrhoea in a Patient with Urticaria Pigmentosa

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Abstract. A patient with urticaria pigmentosa who gave a 40-year history of diarrhoea was found to have systemic mastocytosis with gut involvement. The radiological appearances of the gut in this disease, although not widely recognized, are specific and should be looked for carefully in patients with urticaria pigmentosa who complain of gastro-intestinal symptoms. Gastro-intestinal symptoms, due mainly to alterations in bowel motility or peptic ulceration, are said to occur in some 25-50% of cases of systemic mastocytosis (3, 6). These symptoms have usually been ascribed to generalized histamine release acting on the gut, although cases where mast cell infiltration of the bowel has occurred have also been reported (4, 5). In a review of the radiological features (2), increased gastric rugosity with or without evidence of peptic ulceration and nodular space-filling defects of the bowel mucosa were the most commonly found. Occasionally, diffuse thickening of the wall was seen. It was concluded that these appearance were probably due to local release of vasoactive substances causing submucosal oedema following mast cell accumulation in the gut. Another result of such infiltration may be malabsorption (1).

CASE REPORT

A 64-year-old man had suffered from diarrhoea and a widespread skin rash for 40 years. His rash had become gradually more noticeable over this period and for the last 2 years he had in addition suffered from flushing attacks, last approximately 3 days and occurring once every 2-3 months. His diarrhoea was severe on average once a year. At these times he would produce up to 20 motions a day, sometimes blood-stained. More usually he passed four or five watery stools each day and no treatment appeared to alter this pattern. Twenty years previously he had been told he was suffering from ‘colitis’ after a sigmoidoscope examination, but no histological proof was obtained.

On examination he had a widespread rash consisting of discrete, pigmented telangiectatic macules consistent with the ‘telangiectasia macularis eruptiva perstans’ variant of urticaria pigmentosa. Physical examination revealed 3 cm hepatosplenomegaly. A skin biopsy confirmed an increased number of mast cells in the dermis, while bone marrow biopsy showed focal aggregation of mast cells. Screening for bone involvement was negative, as was the peripheral blood. Five-day faecal fat estimation was within normal limits. Carcinoid syndrome was excluded on the basis of normal urinary 5-HIAA excretion.

Sigmoidoscopy showed an oedematous granular rectal mucosa and gastroscopy revealed a mild gastritis. A barium meal revealed increased rugosity in the stomach and in the duodenum many nodular space filling defects. These ‘indentations’ were seen in several areas of the small bowel on follow through examination, and also in the transverse colon and hepatic flexure following a barium enema. Histological examination of the jejunal and rectal biopsies showed a mixed infiltrate of mast cells and eosinophils.

DISCUSSION

The duration of our patient’s diarrhoea is rather unusual in this disease, but not without precedent. There have been several cases recorded of long-standing gastrointestinal involvement in mastocytosis, the longest of which is 25 years (5). As in our case, there was no evidence of malignant transformation.

Oral disodium cromoglycate has been shown in a double-blind trial to control the symptoms of the disease quite well (7). In our patient the flushing attacks and exacerbations of diarrhoea have disappeared following institution of this drug, although his overall bowel frequency remains three to four stools per day.

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