

Case 1: Urticaria Pigmentosa

Dr. K. Y. Chow

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Physical examination

There were generalized brownish macules and patches over his face, trunk and limbs (Figures 1 and 2). The palms and soles were spared. No blister or bulla was seen. Positive Darier's sign was demonstrated on the lesion.

CASE SUMMARY

History

A six-year-old boy was referred because of generalized itchy erythematous patches over his face, trunk and limbs since four months of age. He felt more itchy when he was hot or after scratching. The lesions noticeably whealed after rubbing. Otherwise he had been healthy all along with normal development. There was no systemic upset, and no gastrointestinal upset or any respiratory problem. There was no similar problem in the family.

Investigations

Complete blood picture and blood biochemistry were normal. The white cell count was normal with no excessive eosinophilia. Skin biopsy showed basal hyperpigmentation of the basal epidermis. There was sparse perivascular mononuclear cell infiltration in the upper half of the dermis. Metachromatic stain showed that most of the infiltrate was composed of mast cells. The histological picture was consistent with urticaria pigmentosa.



Figure 1: Brownish maculopapular rash over the face



Figure 2: Similar rash over the trunk and upper limbs

Treatment

The boy was prescribed with oral antihistamine (hydroxyzine 10mg twice daily) and his itch was well controlled. The parents were advised to keep the boy away from excessive heat, rubbing or hot bath. Avoidance of medications containing aspirin was stressed. They were reassured that this problem would eventually resolve spontaneously in most of the children.

REVIEW ON URTICARIA PIGMENTOSA

Mastocytosis is a disorder of mast cell proliferation, which is usually confined to the skin but may involve all organs except the central nervous system.

Epidemiology

The incidence of urticaria pigmentosa is estimated to be between 1 in 1000 to 1 in 8000 of new dermatology patients, but this figure is probably an under-estimate.¹ The condition affects all races, and does not exhibit any sex predilection. There is no familial predisposition. About 50% of the patients with urticaria pigmentosa have disease onset between birth and two years of age,

while about 75% of the cases occurred before 4 years of age. There is a second peak of incidence in the late third to early fourth decades. In this latter group of patients there is increase risk of systemic involvement. With systemic involvement, there is 30% increased risk of malignant transformation when compared with those cases confined to the skin only.¹

Aetiology

The aetiology is unknown. It is unlikely to be due to dysplasia as most cases regress with age. It may be a hyperplastic response to abnormal stimuli. Mast cell growth factor (MCGF), which stimulates mast cell growth, is identified in increased amount around the lesion. It is produced by keratinocytes and fibroblasts. MCGF also stimulates melanin production by melanocytes.

Clinical features

1. *Urticaria Pigmentosa*

Urticaria pigmentosa typically presents as monomorphic, pigmented maculopapular or nodular lesions, which are usually widespread and symmetrical. Positive Darier's sign may be demonstrated in the lesions. Rubbing and scratching may cause intense itching.

A generalized bullous variety is sometimes seen, and it characteristically occurs in infants. This bullous form is not associated with a poor prognosis. It has been estimated that about 60% of infant or childhood cases may show blister formation in some of the lesions. In most cases, blistering would have subsided spontaneously after 2 or 3 years.²

2. *Telangiectasia macularis eruptiva perstans*

Lesions in this variety are characterized by diffuse red or brownish red macules, consisting of fine telangiectasia. It usually occurs in adults. Pruritus and whealing may be absent. It tends to be persistent and is usually unresponsive to treatment. It runs a benign course and is mainly of cosmetic concern.

3. *Diffuse cutaneous mastocytosis*

In this rare condition, there is diffuse mast cell infiltration of the skin, which has a yellowish, thickened peau d'orange appearance and a doughy consistency. The skin folds in the axillae and groins are accentuated. There is an intense pruritus and large bullae form easily

following mild trauma. This condition has been reported both in adults and in infants. Systemic involvement is common and it carries a 25% mortality rate.²

4. Mastocytoma

In this localized cutaneous form, the lesion is usually a red, pink or yellow nodule. It is usually solitary but occasionally it can be multiple. It usually appears in infancy or childhood. The lesion can wheal when being rubbed and blistering may occur. Occasionally, attacks of flushing can be precipitated when these lesions are rubbed.

5. Systemic mastocytosis

In this condition there is an abnormal increase in mast cells in organs other than in cutaneous tissues. It is estimated to occur in at least 10% of all patients with mastocytosis. Symptoms in this condition may be due to excessive release of mast cell mediators such as histamine and prostaglandin D₂ (PGD₂).³ Symptoms may include flushing, palpitations, hypotension, syncope, wheezing, dyspnoea, nausea, vomiting, abdominal pain, diarrhoea, and bone pain due to skeletal infiltration. Half of the cases have cutaneous involvement. There may be hepatosplenomegaly on physical examination. Haematologically, there may be anaemia, leucocytosis and eosinophilia. Skeletal X-ray may demonstrate osteoporosis or osteosclerotic lesions. Bone marrow biopsy may demonstrate marrow infiltration by mast cells. It has to be noted that systemic symptoms can occur in the absence of extracutaneous involvement.

Differential diagnoses

Mastocytoma has to be differentiated from juvenile xanthogranuloma and spitz naevus. In urticaria pigmentosa, the differential diagnoses include papular urticaria, histiocytosis X, secondary syphilis and papular sarcoid.

Diagnosis

The diagnosis can be established with skin biopsy. There is accumulation of normal looking mast cells in the papillary dermis and perivascular region. In diffuse cutaneous mastocytosis, there is diffuse mast cell infiltration throughout the dermis from epidermis down to the subcutis. Mast cell has a central round nucleus giving rise to the "fried egg" appearance. It contains metachromatically stained (Giemsa's and toluidine blue) granules in the cytoplasm.

Other investigations that can be performed to look for systemic involvement includes skeletal survey, bone scan, bone marrow biopsy, upper endoscopy and liver biopsy.

Management

The parents should be advised on how to avoid potential factors that may exacerbate symptoms, such as temperature changes or skin friction. Drugs like non-steroidal anti-inflammatory drugs, narcotics and alcohol should be avoided as they can destabilize mast cells and cause degranulation.

Oral H₁ antihistamine antagonists such as hydroxyzine and ketotifen are useful for symptomatic control. H₂ antagonist may be beneficial especially if there is gastric hypersecretion. Mast cell stabilizer likes disodium cromoglycate may be used as an adjuvant.

The increase excretion of PGD₂ has prompted trials with aspirin. Some success has been reported but it is important to carry out the trial in places where resuscitative facilities are available. Concurrent administration with H₁ and H₂ blockers is important, because aspirin can potentially destabilize and cause degranulation of mast cells. The present therapeutic role of aspirin in UP is still controversial.

Potent topical steroid under occlusion has been reported to be useful in treating urticaria pigmentosa, but it is only feasible in patients with localized disease like mastocytoma.^{4,5}

Oral PUVA therapy was first reported to be useful in treating urticaria pigmentosa in 1978. The mechanism of action is uncertain. Patients with disease onset during childhood and early adolescence, and patients with skin types I and II respond better to treatment. Bath PUVA is not effective.^{2,6}

Interferon alpha-2b has been tried in patients with systemic mastocytosis, and is found to cause a decline in bone marrow mastocytosis and reduced excretion of histamine metabolites.⁷ However, prolonged therapy is needed and dose-limiting side effects are frequent.

Prognosis

Most childhood onset urticaria pigmentosa resolve spontaneously.⁸ The natural course for adult-onset type

is persistent and stable. However, urticaria pigmentosa occurring in adult has an eight-fold increase incidence of systemic involvement. Approximately 30% of patients with benign, systemic mastocytosis will eventually developed a malignant process. Normal blood cell counts are found only in those patients without malignant transformation. Malignant mastocytosis patients have significantly lower erythrocyte and platelet counts while their leucocyte counts are significantly higher.⁹ The greatest risk for malignant disease is in patients presenting with systemic involvement in late middle-age with the average age for haematological disorder being diagnosed at age 66.¹

Learning points:

Extensive and invasive investigations are not warranted in most paediatric cases of urticaria pigmentosa. However adult cases with systemic involvement should be monitored for malignant transformation.

References

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