MASTOCYTOSIS

REPORT OF A CASE IN A 15½-WEEK-OLD INFANT WITH CUTANEOUS AND GENERALIZED SKELETAL CHANGES

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(RECEIVED FOR PUBLICATION APRIL 13, 1965)

The evolution of medicine has seen the concept of urticaria pigmentosa, as first described nearly 100 years ago by Nettleship (1869), expand to a wide spectrum of disease extending from the simple benign mastocytoma (Marshall, Walker, Lurie, Hansen, and Mackenzie, 1957) to the malignant generalized fatal mastocytosis (Ellis, 1949). Sagher and Even-Paz (1960) cite 15 synonyms which may be included under this heading.

At first the disease was considered to be entirely in the field of dermatology, and many references come from that speciality. However, since Ellis (1949) described a necropsy on a fatal case in a male infant, showing the invasion of many organs by mast cells, and Sagher, Cohen, and Schorr (1952), Sagher, Liban, Ungar, and Schorr (1956), and Sagher and Schorr (1956) noted the radiographic changes associated with this condition, the interest has spread to radiologists, hospital doctors, and paediatricians (Marshall *et al.*, 1957; Rider, Stein, and Abbuhl, 1957; Waters and Lacson, 1957; Lees and Stroud, 1959; Poppel, Gruber, Silber, Holder, and Christman, 1959; Stutzman, Zsoldos, Ambrus, and Asboe-Hansen, 1960; Stutzman and Urbach, 1961; Bigelow, 1961; Szweda, Abraham, Fine, Nixon, and Rupe, 1962; Pastras and Beerman, 1962).

The first descriptions of the basic mast cell were made by Thin (1877) and Ehrlich (1877). Sangster (1878) coined the term urticaria pigmentosa. Unna (1887) described the mast cell infiltrate in the then only known cutaneous lesion. More recently attempts have been made to understand the functions of the basic cell and its evolution from basic cell types (Remy and Herzberg, 1961; Nickel, 1957; Beare, 1958; West, 1958; Head, 1958; Degos, 1960; Padawer, 1963). Bigelow (1961) compares the histiocytoses and mastocytoses, their similarities and differences.

Many unusual findings are noted in patients with

mastocytosis, which are not common to all patients and may not be present at all times in any particular patient. Among them are hyperhistaminaemia, hyperhistaminuria, hyperheparinaemia, capillary changes, gastro-enteric symptoms, spontaneous histamine shock, aspirin sensitivity, coagulation changes, and abnormalities of lipoprotein metabolism. Mastocytosis may also occur without cutaneous lesions and constitutes a diagnostic challenge (Friedman, Will, Freiman, and Braunstein, 1958; Ende and Cherniss, 1958).

The surgical removal of an isolated mastocytoma in a patient with generalized symptoms due to excess histamine release may lead to a dramatic cure of their complaints. There is no specific treatment for other forms of the disease at the present time. Paediatricians should be acquainted with the condition and its vagaries, as 75% of reported cases (which includes benign urticaria pigmentosa) are seen in this age-group: of the paediatric cases, 50% begin in the first six months of life. The majority of these patients have multiple cutaneous lesions which clear completely at puberty.

Eight classifications were offered recently (Ellis, 1949; Sagher, 1956; Nickel, 1957; Marshall *et al.*, 1957; Beare, 1958; Poppel *et al.*, 1959; Sagher and Even-Paz, 1960; Szweda *et al.*, 1962), of which Sagher and Even-Paz (1960) provides the most comprehensive one. He divides the patients into 3 groups: (a) cutaneous, (b) cutaneo-systemic, and (c) systemic.

The radiological changes that may occur are divided into a *generalized* or a *localized type*. The *generalized* type shows generalized cystic osteoporosis of the ribs with thickening of the bony trabeculae, stippling of the bony structures of the skull, and thickening of the skull tables and osteosclerosis of the pelvic bones and vertebrae. The *localized* type shows calcified and decalcified areas which may

FIG. 1.—Anterior view of the patient.

FIG. 2.—Close-up view of lesions on the back of the patient.

occur in humerus, radius, femur, skull, clavicle, and scapula.

The following report is of an infant with disseminated cutaneous and generalized skeletal changes.

Case Report

B.P. (548, 648 H.S.C.), a male infant, born February 3, 1963, after a normal pregnancy lasting 37-38 weeks, birth weight 3.29 kg., was admitted on May 21, 1963, to the Hospital for Sick Children, Toronto, at 15½ weeks of age, because a rash had appeared at 1 month of age. The rash had erupted following the introduction of cereal and orange juice into the diet. The stools became loose and the buttocks reddened at this time. The rash continued to spread; the early pink lesions did not disappear, and as they aged, they became pale brown in colour (Figs. 1 and 2). With the exception of two colds with associated diarrhoea, the infant had had no illness.

Family history indicated that the mother had hay fever and both maternal and paternal grandmothers had asthma.

Examination revealed a body length of 59.7 cm.; head and chest each measured 39.4 cm. The liver was palpable 2.5 cm. below the right costal margin. The cutaneous lesions varied from 4 mm. to 2.5 cm. in diameter. The surface of the lesions was slightly rough. Urtication occurred on stroking the lesions (Darier's sign) which were mauvish brown to pale brown and were distributed over the whole body, but more densely over the head and trunk. No red or pink lesions were apparent, and there were no haemorrhages or bullae.

Laboratory findings are reported in Tables 1 to 4. A skeletal survey in May 1963 revealed a diffuse disturbance of bone growth with dense zones of provisional calcification at the metaphyses of the long bones and dense perimeters around the vertebral bodies, iliac crests, and small bones of the extremities (Fig. 3a-c). Biopsy of one of the cutaneous lesions showed diffuse infiltration of the subepidermis with mast cells. The enlargement of the liver was not apparent at follow-up examination in July 1963, but a small firm raised area, 0.25 cm. in diameter, appeared at the vertex of the skull. In January 1964 the body weight was 10 kg. The liver was again palpable 1 cm. below the right costal margin. The lesion at the vertex had disappeared. Radiographs taken in March 1964 (Fig. 4a-c) showed complete clearing of the bony changes described above. In July 1964, the cutaneous lesions were unchanged, the liver and spleen were not palpable, and the baby was well.

Discussion

As the diverse nature of mastocytosis has become known and since there was a fatality in infancy, there has been reason to admit these patients for investigation.

A review of the patients seen at the Hospital for Sick Children, Toronto, revealed 14 (Tables 1-4). The first was admitted in 1938 and the remainder in the past 10 years. Before 1949 it was felt that most cases occurring in early childhood had a good prognosis and a spontaneous recovery occurred from 6 to 10 years of age. No record of out patients seen

TABLE 1
MASTOCYTOSIS: HISTORY AND PHYSICAL FINDINGS

History No. (H.S.C.)	Year of Diagnosis	Age (yr.) on Admission	Age at Onset of Rash	Family History of Allergy	Allergic Disease in Patient	Other Disease in Patient	Urticaria Pigmentosa	Description of Rash
94759	1938	1 10/12	2 wk.	—	—	Localized convulsive disorder	+	Profuse general maculopapular lesions 1-2 to 5-10 mm. in diameter, light melanotic tint, small raised areas of erythema
189576	1953	3 4/12	8 mth.	—	—	Rt. ptosis, rt. meiosis	+	Rash in diaper area extending to face, trunk, and extremities
251593	1953	2 3/12	4 mth.	—	Eczema	Secondary infection of eczema	+	Generalized rash of irregularly rounded papular brownish lesions
298486	1954	1	Birth	—	—	—	+	Reddish-brown discrete, slightly raised spots on back, chest, neck, and trunk; diaper area and limbs clear
318131	1955	1 4/12	1 mth.	Hay fever, asthma	—	—	+	Generalized rash except palms of hands
339173	1956	4/12	2 mth.	—	Urticaria	—	+	Rash on chest, trunk, neck, upper arms, and legs
389993	1958	6	—	—	—	Convulsive disorder	+	Pigmented papules, pink to brown over scalp, trunk, neck, forearms, and thighs
412417	1959	1 6/12	—	—	—	—	+	Rough slightly raised reddish area on left foot (mastocytosis)
430824	1959	6 3/12	3 yr.	—	Urticaria	? Addison's disease	+	Spotty brown rash
433742	1959	6 7/12	18 mth.	—	—	Nephrosis	+	Rash over trunk, upper parts of arm, around neck, a few papules over trunk
449701	1960	1 2/12	3 mth.	—	—	Pyloric stenosis	+	Small macular reddish to yellowish-brown rash on trunk, limbs, lower face, and neck
502944	1961	3/12	6 mth.	—	—	—	+	Red macular rash in diaper area, spreading over body, more numerous in creases
481643	1961	7/12	4 mth.	—	—	—	+	Rash in diaper area and chest, nodular in nature, lesions 2 to 8 mm. diameter; also fine macular rash on chest and abdomen
548648	1963	4/12	1 mth.	Hay fever, asthma	—	—	+	Macular, profuse, discrete, pink to mauvish brown rash; lesions 6 mm. to 2.5 cm. diameter, on trunk, scalp, and face; few lesions on extremities

TABLE 2
PHYSICAL AND LABORATORY FINDINGS

History No. (H.S.C.)	Urtication (Darier's sign)	Pruritus	Dermographism	Spleen	Liver	Biopsy	Radiographs	Wassermann	TB Test	Urine	EEG
94759	Yes	—	+	—	—	0	0	— ve	— ve	— ve	'Non-specific changes'
189576	Yes	—	—	—	—	+ ve	Chest — ve; long bones — ve	0	— ve	— ve	
251593	—	—	—	2 cm.	2 cm.	+ ve	0	0	— ve	— ve	
298486	—	—	—	—	—	— ve	0	0	— ve	— ve	
318131	—	—	—	—	—	0	0	0	— ve	— ve	
339173	—	—	—	—	—	0	0	0	0	Albumin trace; occas. WBC	
389993	Yes	—	—	—	—	0	Skull — ve; ankle — ve	0	— ve	— ve	
412417	No	—	—	—	—	+ ve	0	0	0	— ve	
436824	No	—	—	—	—	0	Chest — ve; IVP — ve; skull — ve	0	— ve	— ve	
433742	Yes	—	—	—	—	±	Hands — ve; skull — ve; chest — ve; IVP — ve	0	0	Albumin + + ; occas. epith. cells	
449701	—	—	—	—	—	0	0	0	0	— ve	
502944	Yes	—	—	—	3 cm.	+ ve	Chest — ve; long bones — ve	0	— ve	— ve	
481643	—	—	—	—	2 cm.	+ ve	Chest — ve; skull — ve	0	— ve	— ve	
548648	Yes	—	—	—	2.5 cm.	+ ve	Skeletal survey + ve	0	— ve	— ve	

History No. (H.S.C.)	Hb (g./100 ml.)	RBC 10 ⁶	WBC 10 ³	Platelets 10 ³	Neutrophils	Bands (%)	Eosin (%)	Lymphocytes (%)	Monocytes (%)
94756		4.5	8.5		35			65	
189576	12.4	4.3	8.4	N	41	2	2	42	12
257893	9.5		19.6						
298486	13.6		20.3	N	53	1	2	38	6
318131	12.9		17.2	N	60	5	2	32	1
339173	12.7		9.8	214	28	0	1	68	3
389993	12.8		10.5	N	54			45	1
412417									
430824	12.0		5.3		48		2	49	1
433742	13.9		9.2	370					
449701	11.8		9.5		41	3		51	5
502944	8.6		12.8						
481643	12.3		14.9		33		1	61	5
548648	10.6		19.0	603	25	7	5	55 (11% atypical)	5

but not admitted has been kept, and more cases have been seen at this hospital than this report indicates.

One child had a solitary mastocytoma, the remainder had urticaria pigmentosa. The age range at the time of admission was 4 months to 6 years and 7 months. There were 9 boys and 5 girls. The onset of the rash was recorded in 12 cases: 8

were 6 months or under, 2 were 6 to 12 months, one was 18 months, and one was 3 years. A family history of hay fever with asthma was recorded in 2 patients. One patient showed dermographism, none had pruritis, 2 had simple urticaria, and one had eczema in addition to urticaria pigmentosa. Other organic disease was present in 6 patients, 2 with

FIG. 3.—Radiographs taken May 1963, showing dense perimeters of calcification around the vertebral bodies (a); the iliac crests (b); and around the small bones of the hands (c).

INVESTIGATIONS

Plasma Cells (%)	Basophils (%)	Metamyelocytes (%)	Smear	Reticulocyte Count	ESR (mm./hr.)	Bleeding Time	Clotting Time	PTT (sec.)
1			RBC, slight anisocytosis; WBC, atypical; lymphocytes present					
			RBC, slight hypochromasia; WBC occas. atypical lymphocyte RBC normal WBC neutrophilia Smear normal			2 min. 45 sec.	6 min. 25 sec.	
			Slight lymphocytosis		8 30	1 min. 15 sec.	5 min. 30 sec.	
			Differential normal	2.6				
	2	1	RBC, slight hypochromia; occas. poikilocytosis and polychromasia					53

TABLE 4
BONE-MARROW DIFFERENTIAL COUNTS PER 100 CELLS IN 2 CASES*

History No. (H.S.C.)	Bone-marrow	Myelocytes	Meta-myelocytes	Bands	Eosinophils	Poly-morphs	Lymphocytes	Mast Cells	Erythroid Elements	Blasts
433742	Positive	10	13	22	4	16	12	3	20	0
548648	Negative	9	16	21	0	13	23	0	17	1

* In one other case (251593) bone-marrow cell count showed normal proportions of white cells, megakaryocytes, platelets, and red blood cells.

FIG. 4a-c.—Radiographs taken in March 1964, showing complete clearing of the bony changes.

convulsive disorder, one with nephrosis, one with possible Addison's disease, one with secondarily infected eczema, and one with pyloric stenosis. In 8 patients, the central portions of the body (head and trunk) were more affected. In 3 patients the rash was more prominent in the diaper area. In one, none was present in this area. The nodular or papular nature of the rash was mentioned in 7 patients. Red, reddish, pink, mauve, brown, and melanotic colorations were described. Enlargement of the spleen was noted in one and an enlarged liver in 4 patients. Albuminuria was noted in 2 (one with nephrosis). Biopsy was performed in 8 patients and was positive in 6, negative in one, and questionable in one. Bone-marrow study of 3 patients gave positive findings (excessive mast cells) in one, and negative findings in 2. Radiographs in 7 patients revealed one with bony change. Anaemia was present in 2 and a leucocytosis of more than 10,000 cells/c.mm. in 7. An excess of platelets was observed in one patient. Eosinophils were raised in one; another showed plasma cells in the peripheral blood smear; and atypical lymphocytes were described in 3 patients.

A search of the published reports revealed 12 paediatric patients with cutaneous and bone lesions. Of these, 9 showed solitary or localized skeletal lesions (Asboe-Hansen, 1953; Grupper, 1954; Shair and Casper, 1955; Gulden and Niebauer, 1956; Edelstein, 1956; Remy, 1957; Hasselmann and Scholder-Oehmichen, 1957; Lees and Stroud, 1959; Niordson, 1962); and 3 showed the generalized type of skeletal lesion, the youngest of whom was 2 years old (Rider *et al.*, 1957; Lees and Stroud, 1959). The case reported here appears to be the youngest to show generalized skeletal lesions, and is unusual in that the radiographic changes completely disappeared by 17 months of age.

On reviewing the description of patients with mastocytosis but without cutaneous lesions, one wonders if some of the infants or small children with general or local pruritis, but no cutaneous lesions other than self-inflicted scratch marks, may not have systemic mastocytosis without skin lesions. Complaints such as flushing, sweating, and fainting, frequently may suggest this diagnosis and warrant more investigation than these symptoms are commonly accorded.

Summary

A brief discussion of mastocytosis is presented.

An infant less than 4 months old with cutaneous and skeletal asymptomatic mastocytosis is described.

The skeletal lesions in this patient apparently cleared entirely with growth.

The records of 14 patients with this condition admitted to the Hospital for Sick Children (1938-1963) are reviewed.

I wish to thank Dr. J. H. Ebbs for reviewing this report.

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