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Congenital Gigantism of Peroxidase Granules*

The First Case ever Reported of Qualitative Abnormity of Peroxidase

By

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The present case is, I believe, worthy of report because of a *monstrous* malformation of peroxidase granules of blood leucocytes. The peroxidase reaction I used is that sensitive method of Sato-Sekiya's peroxidase stain.[1] In spite of the fact that this method is now widely used, —many books on hematology and diagnostics recommend the use of it,—such a case has not been reported within my knowledge. I presume the present case will be the very first case ever reported of *qualitative* peroxidase abnormity.

Case Report

T. K. an 11 month old Japanese male infant, was admitted to the Tohoku University Hospital on December 2, 1950, because of an abdominal distention and an acute upper respiratory tract infection.

Explanation to the pedigree of the present case (Cf. Fig. 1): Parents are of consanguinous marriage. One elder brother (Fig. 1, V_1) died in the second year of life and two sisters (Fig. 1, V_3 and V_6) in the third year during some infection. Whether these three cases showed an abnormity of peroxidase granules is unfortunately unknown. But these brothers and sister had in common with the present case: photophobia, pale color of the hair, pigmentation of uncovered parts of skin, frequent occurrence of pustules with generalized lymphadenopathy and marked abdominal distention with hepatosplenomegaly.

History of the present case: The mother's pregnancy was uncomplicated. The patient was born at term with normal delivery. The weight was 2800 g.. At birth the pale color of the hair and the skin was noticed. Until five months of age, besides photophobia, dark pigmentation was noticed on the face and the back of hands and feet and simultaneously a more or less darker pigmentation of hair was noticed. His growth and development were

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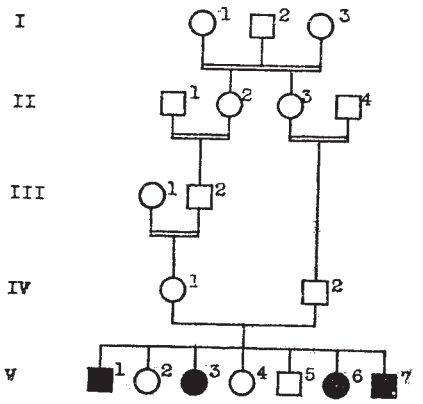


Fig. 1. The pedigree of the present case. Explanation to the pedigree:
V_1, V_3, V_6 . . . . . fatal before full 3 years of age.
V_7 . . . . . the present case.
The pedigree is reliable only as to V. As for I–IV, the mother of the present case did not know the details, so that it is probable that in each of the generations I–IV there was one or some infants who had died young.

rather retarded, as he was able to sit by himself only at nine months of age. He was 11 months old when he was admitted to our Hospital and then he could neither creep nor stand even with support. At 7 months of age, he had pustular lesions on the trunk with formation of ulcers and scars and with concomitant enlargement of superficial lymphnodes. During the time the abdomen had been gradually distended. Five days prior to admission, he had a high temperature up to 38°C, mild cough, loss of appetite and became distinctly prostrated. The mother was afraid that the child might die of the present illness, because she had already experienced the death of three other children of hers who had succumbed to a similar affection, and she brought the present case to the Hospital in the hope that something would be done to save him from death.

Physical examination: The physical examination upon admission revealed a fairly well developed and seriously ill infant. Measurements were 8640 g. in weight (normally 8920 g.), and 45.5 cm, 47 cm and 44.7 cm in circumferences of head, chest and abdomen respectively. His facial expression was mask-like. The hair of his head and eyebrows were whitish grey. The diagnosis of xerodermia pigmentosum was confirmed by Dr. M. Ito, Professor of Dermatology. The brown pigmentation was noticeable in the peripheral part of the face, especially distinct in subauricular regions. The mucous membrane of the upper lid appeared pale. The buccal membrane was free from pigmentation. The tongue seemed to be rather too large. The dark pigmentation of the skin was noticed on the extensor side of the four extremities too. The ophthalmoscopic examination revealed the presence of albinismus fundi oculi utrisque (Prof. Y. Hayashi of Ophthalmology). The skin was sweating, but not itching. There was a generalized lymphadenopathy (cervical ##, cubital +, occipital + and inguinal +) and the coccygeal region was eczematous. Lungs and heart were clear. The pulmonic second sound was

accentuated. The pulse was 102 and the respiration 44 per minute. The blood pressure was 120 systolic and 70 diastoric. The abdomen was moderately distended. The fluctuation was negative, while flanks were dull on percussion. The liver was palpable 2 fingers breadth below the right costal margin, with smooth surface and firm consistency. The spleen was remarkably enlarged, extending up to two fingers breadth below the umbilicus, with smooth surface and firm consistency. The deep tendon reflexes were normal.

Laboratory findings upon admission: The stool was guaiac negative. The urobilinogen was slightly positive in urine. The X-ray of long bones showed epiphyseal transversal lines. The X-ray of the skull and of the hip joints were negative.

Course of illness (Cf. Fig. 2. Table I. Table II): During hospitalization, he ran irregular fever up to 39°C, as is shown in Fig. 2. From the second hospital day on, a daily dose of 200,000 units of penicillin was given intramuscularly for ten days without effect.

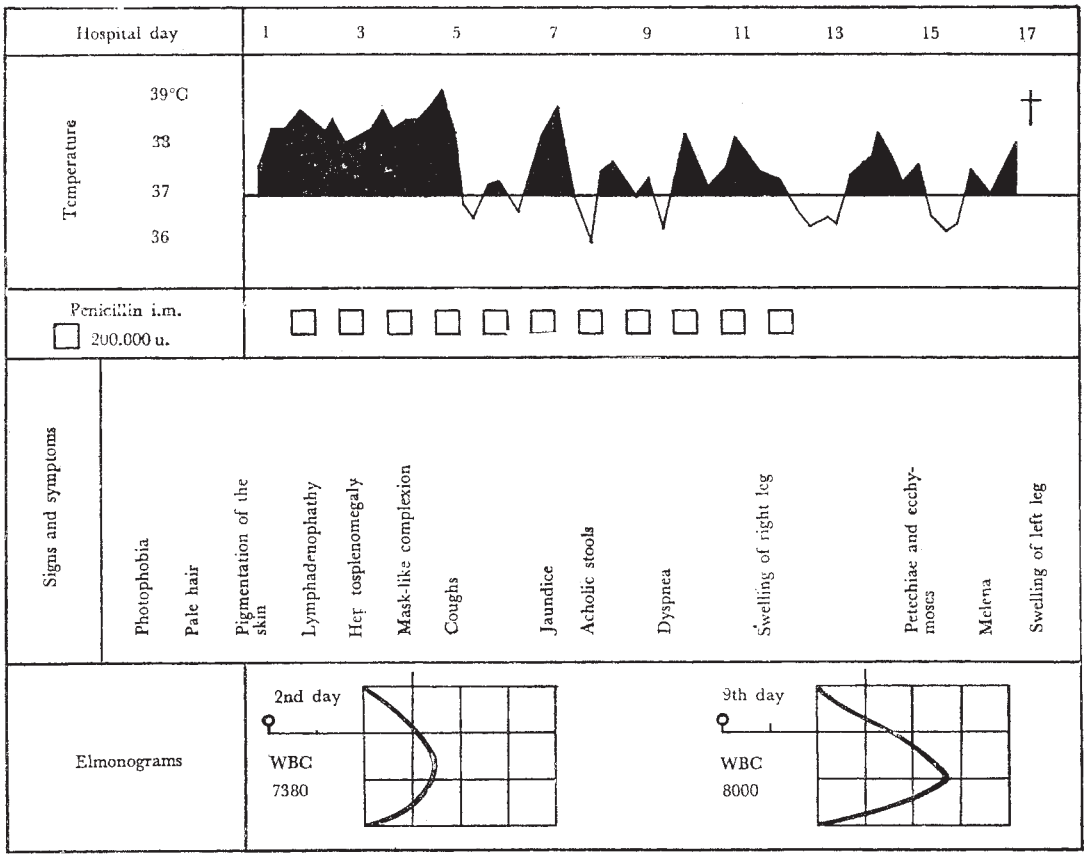


Fig. 2. The course of illness of the present case.

On the second hospital day, blood examination revealed a marked neutropenia with the characteristic abnormity of peroxidase granules of leucocytes which will be described in detail in the following chapter. RBC was 4,100,000, Hgb. 10.8 g/dl, platelets 180,000, bleeding time 3 minutes and Rumpel-Leede's phenomenon was positive. On the 5th day, icterus index of blood serum was 13, v.d. Bergh prompt direct positive. Takata-Ara reaction ##.

TABLE I

Blood Counts of the Present Case

Date 1950		Dec. 3	10	18
Hospital day		2	9	17
WBC*	/cmm	7380	8000	14300
Basophils	/cmm	0	0	0
Eosinophils	/cmm	0	0	0
Lymphocytes	/cmm	6130	6560	4720
Monocytes	/cmm	590	1160	1070
Neutrophils	/cmm	660	280	8500
Juvenile forms	%	35	.....	4
Band forms	%	45	30	15
2 segmented forms	%	20	45	40
3 segmented forms	%	0	25	31
4 segmented forms	%	0	0	9
5 segmented forms	%	0	0	1
Nucleated RBC	/cmm	present	present	1680
RBC	millions/cmm	4.10	3.40	2.20
Hgb	g/dl	10.8	8.3	5.5
Color index		0.87	0.81	0.83
Platelets	thousands/cmm	180	.....	36
Bleeding time	minutes	3	(120)	.....
Coagulation time	minutes	4～9	.....	.....
Rumpel Leede's phenomenon		positive	.....	.....

* The differential leucocyte picture was shown by way of Elmonogram (Cf. Fig. 2). The Elmonogram was devised in 1947 by Sato and Hayashi.[6]

On the 7th hospital day, bleeding time was prolonged to 2 hours, and he became anemic and dyspneic. On the same day, he developed jaundice with acholic stools and bilirubinuria.

On the 9th day, RBC was 3,400,000, Hgb. 8.3 g/dl, WBC 8,000/cmm neutrophils 280/cmm. The sternal puncture was performed. The myelogram did not show any leukemic proliferation of single type of cell (Cf. Table II), but the qualitative abnormity of peroxidase granules of leucocyte precursors was the most outstanding characteristic feature.

On the 13th day, a marked swelling of right lower leg with tenderness but without redness and local heat was noticed, and it extended to the thigh in the following two days.

On the 15th day, petechiae and ecchymoses appeared on the right flank and they increased in number and spread far and wide on the entire body surface in the following days.

On the 16th day, he passed two tarry stools. The fontanel was sunken and the oral membrane was dry. He was more anemic and went progressively

TABLE II

Bone Marrow Picture of the Present Case

I.	Total nucleated cell count	28800 per cmm.
II.	Erythropoiesis	
	Proerythroblasts	2.8%
	Normoblasts	58.0%
	Mitotic forms	0.1%
III.	Leucopoiesis	
	Neutrophils	
	Myeloblasts	4.3%
	Early myelocytes	4.1%
	Intermediate myelocytes	10.1%
	Late myelocytes	8.0%
	Bands	0.8%
	2 segmented forms	0.2%
	Eosinophils	
	Myeloblasts	0.2%
	Early myelocytes	0.7%
	Intermediate myelocytes	0.4%
	Late myelocytes	0.5%
	Bands	2.3%
	2 segmented	1.7%
	Monocytes	
	Monoblasts	0.4%
	Monocytes	0.1%
IV.	Reticuloendothelial cells	
	Lymphoid reticulum cells	1.8%
	Lymphocytes	2.9%
	Plasmacellular reticulum cells	0 %
	Plasma cells	0.1%
	Mitotic forms	0.1%
V.	Thrombopoiesis	
	Megakaryoblasts	0.3%
	Megakaryocytes	0.1%
VI.	Myeloid-Erythroid ratio	0.7:1.0

downhill.

On the 17th day, the left leg was swollen as well as the right. RBC was 2,200,000, Hgb 5.5 g/dl, WBC 14,300/cmm, neutrophils 8500/cmm (terminal leucocytosis) and platelets 36,000/cmm. He became apathetic and died.

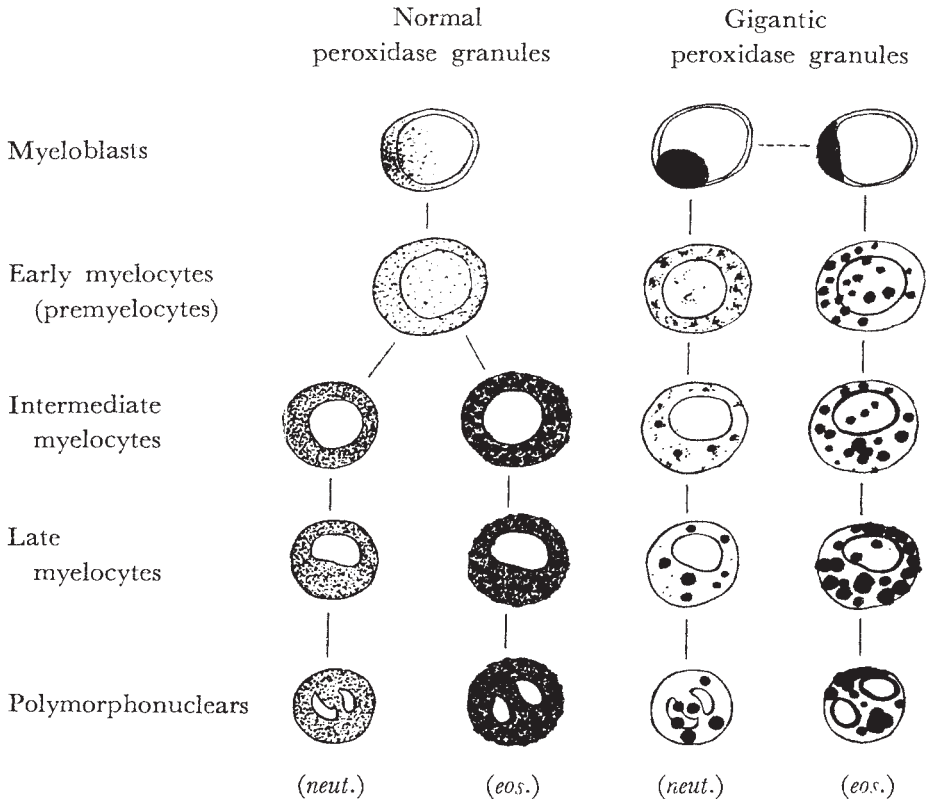
Blood Pictures of the Present Case

Method: The blood or/and bone marrow specimens were stained by the following three methods: Sato-Sekiya's peroxidase method, the Giemsa method and the supravital method with neutral red respectively.

Results: I. Peroxidase stain (Cf. Fig. 3. Fig. 4 and Fig. 5.)

1) Neutrophils: Under Sato-Sekiya's peroxidase stain method, the cytoplasm of normal neutrophils is, as is well known ,entirely filled with fine peroxidase granules. The neutrophils of the present case, however, have scarcely any peroxidase granules except in some limited parts of

Fig. 3



their cytoplasm, while almost all peroxidase granules aggregate very compactly, each group forming a colossal mass, " Gigantic Peroxidase Granule " (G.P.G.). This is spherical or oval, 1 to 3 μ in diameter, or rarely spindle-like in shape, appearing intensely blue and is contained in one cell in the number of 1 to 7. Some of the G.P.G. may coalesce to each other. There may be among the G.P.G. in the cytoplasm a few safranophilic brownish red granules, which give no peroxidase reaction.

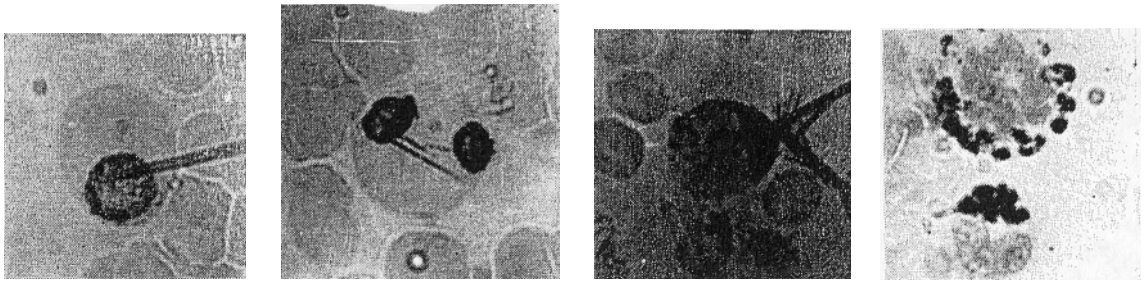
2) Eosinophils: The eosinophils were almost absent in the peripheral blood and were present in the aspirated bone marrow. In the cytoplasm of normal eosinophils, the coarse peroxidase granules are themselves groups of granules, each group appearing to be one coarse peroxidase granule, but they do not make large compact masses. In the present case, however, the cytoplasm is filled with ball-like masses of peroxidase granules i.e. the G.P.G. of various size, 3 to 4 μ in diameter. And the cellular outline seems to be formed by a chain of the G.P.G..

3) Monocytes: Normally the peroxidase granules of monocytes are smaller in size than those of neutrophils. But, in the present case, the overwhelming majority of monocytes have in the cytoplasm the G.P.G. very similar to those of neutrophils described above.

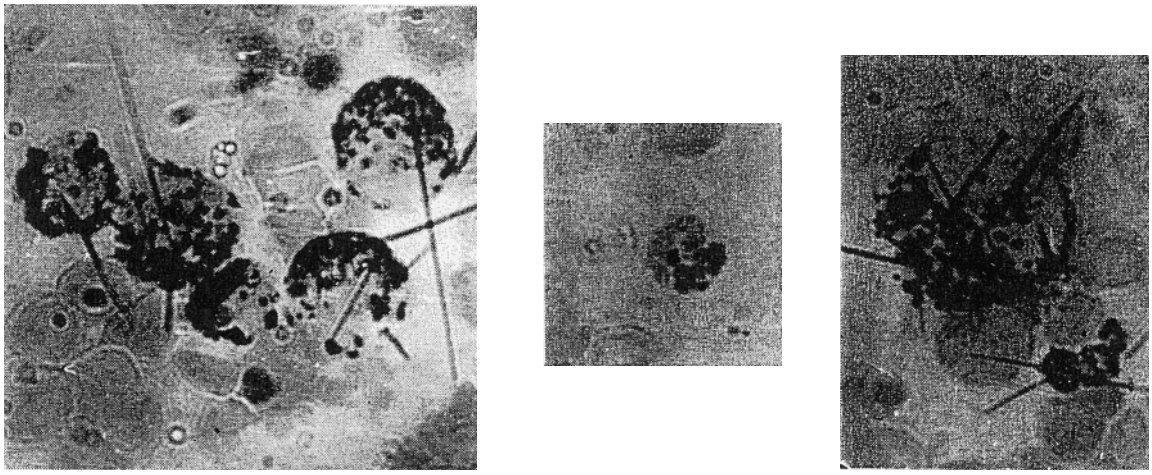
4) Lymphocytes: They show no peroxidase granules. It should also be noticed that there is not any safranophilic granule in their cytoplasm.

Fig. 4 (A). Explanation to all the pictures A.
G.P.G.(s).....gigantic peroxidase granule(s)

A, 1 A, 2 A, 3 A, 4



A, 5 A, 6 A, 7



A, 1., Myeloblast with single gigantic peroxidase granule aggregate with a peroxidatic needle. In fresh specimens, the entire round field of such G.P.G. would be entirely filled with fine blue peroxidase granules. The nucleus is indented due to the presence of the G.P.G..

A, 2., Myeloblast with two G.P.G.s with needle formation. One G.P.G. with needle formation.

A, 3., " Eosinophilic " myeloblast. In this cell peroxidase granules are aggregated, filling the entire space of cytoplasm together and looking crescent-shaped. Needle formation is seen.

A, 4., Myelocyte (upper) in mitosis with a chain of G.P.G.s and neutrophilic metamyelocyte (lower) with clumping of G.P.G.s.

A, 5., Myelocytes, probably neutrophilic, containing numerous G.P.G.s instead of normal-sized fine peroxidase granules. Differentiation between neutrophils and eosinophils is difficult in these cells.

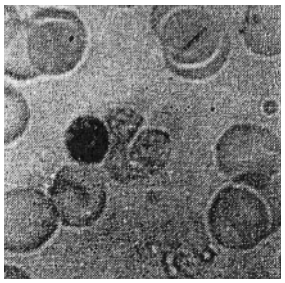
A, 6., Polymorphonuclear neutrophil containing about 10 G.P.G.s in cytoplasm.

A, 7., Early myelocyte (upper) with numerous G.P.G.s covering a part of nucleus. Eosinophilic metamyelocyte (lower) with several G.P.G.s.

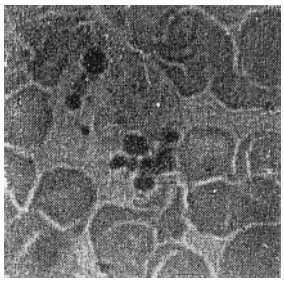
5) Neutrophilic myelocytes: The late and intermediate forms of the cells showed a definite inclination to develop the G.P.G. in their cytoplasm, while each of these G.P.G. is smaller and less characteristic

Fig. 4 (A)

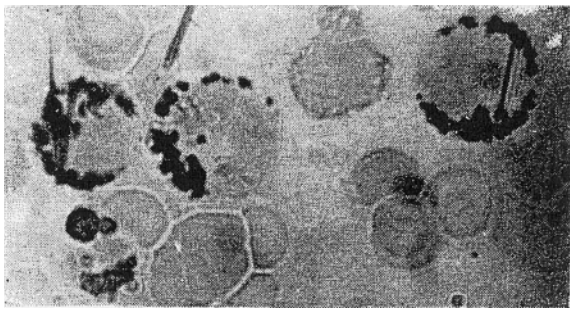
A, 8



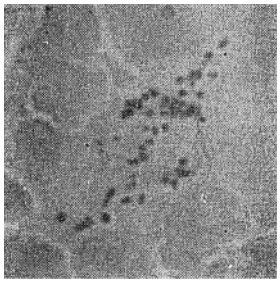
A, 9



A, 10



A, 11



A, 8., Monocyte or neutrophil with single G.P.G..

A, 9., Monocyte with several G.P.G.s.

A, 10., Three early myelocytes (upper) with peripheral G.P.G.s. Probably eosinophil metamyelocyte with G.P.G.s filling two corners.

A, 11., Reticulum cell (star-shaped) with many G.P.G.s. (Normally peroxidase-negative. Even if peroxidase-positive in pathologic cases, peroxidase granules would be only small.)

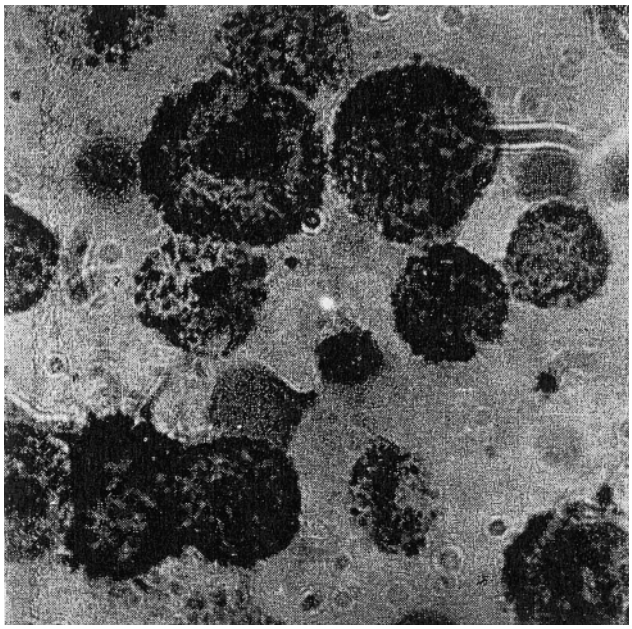
than that of polymorphonuclear neutrophils. There are also a moderate number of intermediate forms between normal sized (or small) peroxidase granule and the G.P.G.. In the early myelocytes, there are typical G.P.G. which are larger in size, less in one cell than those of polymorphonuclears.

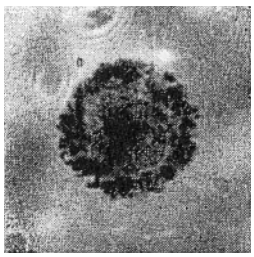
6) Eosinophilic Myelocytes: The majority of the cells of late, intermediate and early stages are loaded with the G.P.G. which are more spherical, and plumper than those of neutrophilic myelocytes and filling the most part of the cytoplasm, covering the nuclei partly.

7) Myeloblasts: In a normal myeloblast, most of the peroxidase granules in the cell are only on one side or in one corner (or in two opposite corners) of the cell, and from such a corner a more or less small number of the peroxidase granules seem to be located radiating toward the equatorial part of the cell. In the present case, the localization of peroxidase granules is limited in one corner or in two opposite corners as in the normal case or occasionally in four corneres of the cell, while, the granules aggregate more or less densely to build a round colossal

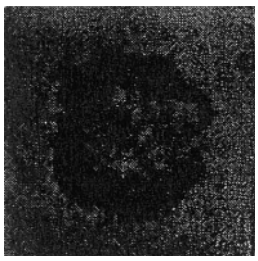
Fig. 4 (B). Explanation to all the pictures B.
These pictures represent normal cases, so G.P.G. does not occur here.

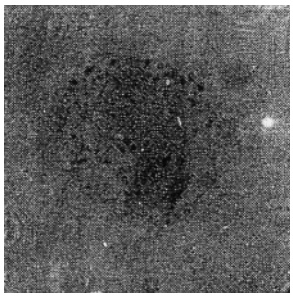
B, 1 B, 2

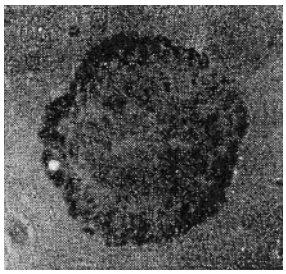


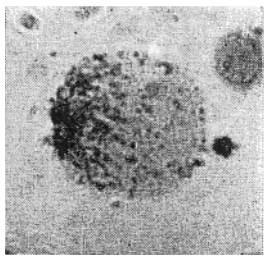


B, 3 B, 4 B, 5 B, 6









B, 1., The bone marrow peroxidase picture of a normal case. The peroxidase granules of these cells are fine and rather diffusely scattered in cytoplasm. One eosinophil myelocyte, which is more heavily loaded with peroxidase granules, is seen in the left lower corner.

B, 2., Neutrophil leucocyte B, 3., Eosinophil leucocyte
B, 4., Monocyte B, 5., Early myelocyte
B, 6., Myeloblast

mass, deserving the name of G.P.G. ever more, a veritable monstrous peroxidase mass. The G.P.G. varies in size, mostly 5 to 10 μ and rarely 2 to 3 μ, and the nuclei of some myeloblasts are indented by the presence of the G.P.G.. Some of G.P.G. are found within vacuoles. In some of the myeloblasts, probably " eosinophilic " myeloblasts, peroxidase granules are aggregated, filling the entire space of one corner of the cell and looking crescent shaped. Peroxidase-negative myeloblasts are occasionally seen.

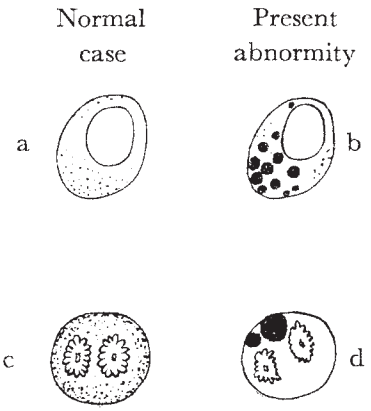


Fig. 5. Gigantic Peroxidase Granules (G.P.G.) in the monocyte and the early myelocyte in mitosis.
a: Normal monocyte, b: Monocyte with G.P.G.s, c: Normal premyelocyte in mitosis, d: Mitotic form of premyelocyte with G.P.G.s.

8) Erythroblasts: All of the erythroblasts examined are apparently peroxidase-negative, but one cell which is peroxidase-positive contained a single spherical G.P.G. in the cytoplasm.

9) Megakaryocytes: All of them examined are peroxidase-negative.

10) Extracellular G.P.G.: They occur very rarely in the blood film and not infrequently in the bone marrow smears, and their size and shape were various as well as those in the cells, suggesting that some of the G.P.G.s could be liberated from the cells of each stage of the cellular development, thus the cells probably subjected to a rapid disintegration.

II. Giemsa stain (Cf. Fig. 6 and Fig. 7)

1) Neutrophils: In most of the neutrophils, there are several round aggregates of the fine violet-pink granules, which look somewhat like small plateletes in appearance. And, among these abnormal aggregates in the cytoplasm, almost none of the specific granules is found to be scattered freely.

2) Monocytes: In the basophilic cytoplasm, there are several round colorless spots, in each of which a group of fine lilac granules occurs as aggregated. Non-aggreagated, free granules are very few in number.

3) Lymphocytes: The cytoplasm contained a large round purplish red or azurophilic body, which was 1 to 3 μ in diameter.

4) Eosinophils: The specific granules are in general, much plumper than normal and different in size in one cell, varying 1 to 4 μ in diameter. These granules are mostly spherical, but some of the largest ones appear rather polymorphous, presumably showing coalescence of two to three original less large, spherical granules. Some of the cells are heavily loaded with these abnormally plump granules.

5) Neutrophilic Myelocytes: The cytoplasm of late myelocytes

Fig. 6

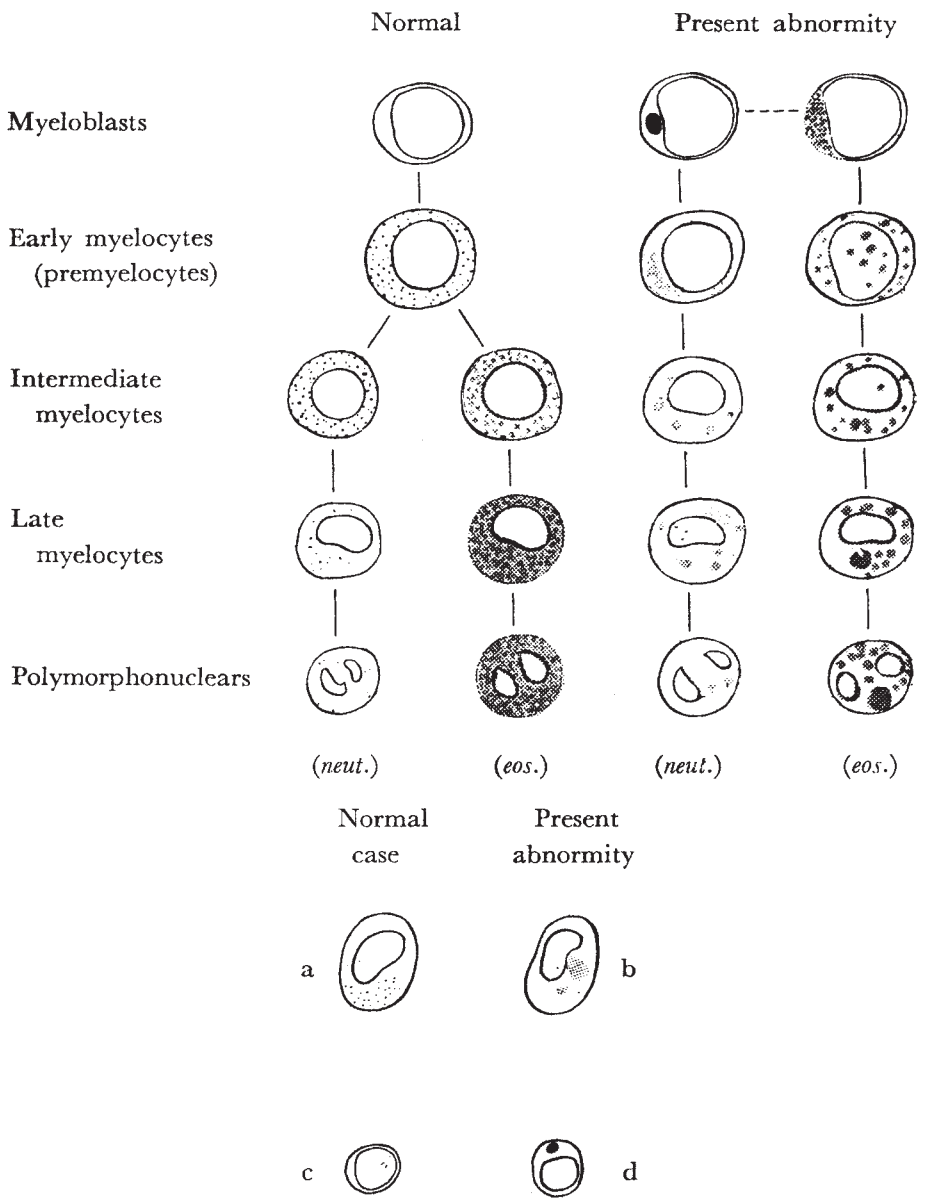


Fig. 7. Abnormal granules in monocyte and lymphocyte (Giemsa stain).

a: Normal monocyte, b: Abnormal monocyte showing clumping of granules, c: Normal lymphocyte, d: Abnormal lymphocyte with a large azurophilic granule.

contained multiple round aggregates of neutrophilic granules almost similar to those found in polymorphonuclears, while the latter is a little more conspicuous. The intermediate myelocytes have a few coarse azurophilic granules, and besides, the cytoplasm shows multiple vacuolization and some of the vacuoles appeared diffusely light reddish yellow or lilac. The early myelocytes (or premyelocytes) have a few fragmented, very coarse granules, appearing purpurish red or azurophilic.

The cytoplasm shows not infrequently marked vacuolization and some of the vacuoles are filled with some material appearing very faintly orange-colored. In some of the cells, the granules are smaller in size and spherical or somewhat needle-like in shape and present in a larger number.

6) Eosinophile myelocytes: They show almost similar abnormity of the specific granules to those of mature eosinophils, while it is noticed that, the apparently younger the cell, the less characteristic is the abnormity of the granules.

7) Myeloblasts: Myeloblasts with " huge azurophilic " granules; they have an extraordinally large round vacuoles in intensely basophilic cytoplasm, which contains round purpurish red granules. These huge azurophilic granules or inclusion bodies are varied in size, 3 to 7 μ, correspondinly to the size of vacuoles, and they are usually round but occasionally appeared modified.

Myeloblasts with eosinophilic granules: They contain definitely eosinophilic granules, which are spherical and less than 1 μ in diameter forming a crescent-shaped space filled with eosinophilic granules in one corner of the cell.

Myeloblasts without granulation are occasionally seen and some of them have large vacuoles only.

8) Neither erythroblasts nor megakaryocytes show particular abnormity, while both of them showed pathologic regeneration. The megakaryocytic picture is identical with that of idiopathic thrombocytopenic purpura, characterized by the presence of immature megakaryocyte containing giant platelet in the strongly basophilic cytoplasm.

In the bone marrow smears, extracelluar eosinophilic granules are found not infrequently.

9) As to nuclear structure, the staining of chromatin is rather weak, esp. in some myeloblasts and early myelocytes, though in a few others chromatin is rather dark stained. In many myeloblasts and early myelocytes there are a larger number of nucleoli, some of which are more or less large and polymorphous.

III. Supravital method (Cf. Fig. 8)

This revealed a peculiar behavior of neutral red vacuoles in neutrophils, monocytes, lymphocytes and red blood corpuscles. Almost immediately after blood smear was prepared, large spherical neutral red vacuoles appeared in the cytoplasm of these cells. In neutrophils and monocytes, the vacuoles are 1 to 3 μ in diameter and occur up to 10 in number in a single cell. In lymphocytes and erythrocytes, vacuoles are less than 2 in number, usually only one in number in a single cell.

IV. The Oxidase Reaction

The oxidase reaction was examined by the Winkler-Schultze method.

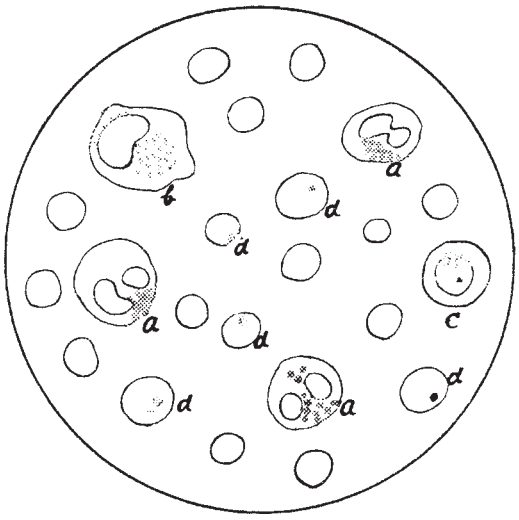


Fig. 8. Peculiar neutral red vacuoles or granules. The peculiar behavior of neutral red vacuoles under the supravital method.
a: Neutrophils showing clumping of neutral red vacuoles in the cytoplasm, b: Monocyte, c: Lymphocyte, d: Erythrocytes.
The neutral red stained vacuoles or granules of erythrocytes of this case were considered to be a characteristic features of the present abnormity manifested in the cells. It is interesting to not that none of the Howell-Jolly bodies was found in the Giemsa stained blood smears of this case.

This, too, revealed a remarkable malformation of oxidase granules of leucocytes, apparently very similar, in size, (group of granules) and localization in cytoplasm in each developmental stage of granulocytes, to those of peroxidase granules i.e. the G.P.G.. In fact, there was no much difference between the oxidase picture and the peroxidase picture except for that each group of oxidase granules showed more clearcut round outline than that of peroxidase granules. I desire to suggest the designnation of Congenital Gigantism of Oxidase Granules for this qualitative abnormity of oxidase granules of leucocytes.

Remarks

The abnormity of different cells under the peroxidase, the Giemsa and the supravital stain methods is summarizingly shown in Table III.

Discussion

A. Sato, the former professor of our Pediatric Clinic, held the chair of Pediatrics from 1917 to 1948. He published his peroxidase reaction in collaboration with S. Sekiya[1] in 1926. But they devised the method already in 1920, so that Sato's work with this peroxidase method continued from this year to 1948—thus as long as almost 30 years. But he had not

TABLE III

The Abnormity of Different Cells under the Peroxidase*, the Giemsa and the Supravital Stain Methods

		Peroxidase stain (Sato-Sekiya's method)		Giemsa stain				Supravital stain with neutral red
		"G.P.G."		aggregates of neutrophilic granules	plumper eosinophilic granules	large azurophilic granules		abnormal vacuoles
		10–5μ	4–1 μ			4–7 μ	1–3 μ	
Leucon	neutrophils							
	polymorphonuclears	—	++	++	—	—	—	++
	myelocytes	—	+	+	—	—	—	?
	eosinophils							
	polymorphonuclears	—	+	—	++	—	—	?
	myelocytes	—	+	—	+	—	—	?
	basophils	?	?	—	—	?	?	?
	promyelocytes	+	+	+	+	+	+	?
	myeloblasts	++	+	—	(+)	++	+	?
	monocytes	—	+	+	—	—	—	+
	lymphocytes	—	—	—	—	—	+	+
Erythron	erythrocytes	—	—	—	—	—	—	+
	juvenile erythrocytes	—	—	—	—	—	—	+
	normoblasts	—	(+) very rare	—	—	—	—	?
	proerythroblasts	—	—	—	—	—	—	?
Thrombon	platelets	—	—	—	—	—	—	?
	megakaryocytes	—	—	—	—	—	—	?
	promegakaryocytes	—	—	—	—	—	—	?
	megakaryoblasts	—	—	—	—	—	—	?
Extracellular granules		+	+	Uncertain	+	—	+	?

* Oxidase reaction presents the same picture as the peroxidase as to the distribution.

come across such a case as I have described above. From the European continent[2] where the above mentioned peroxidase reaction (under the name of "Sato's oxidase reaction or Sato's peroxidase method") has been much in use and from the American continent[3] where the reaction has been much used under the name of "Sato and Sekiya's stain", there has been no report whatever of such a case as my own.

As to the quantitative abnormity or monstrosity, Sato[8] has already reported repeatedly. (He will write, so I am told, systematically about

the quantitative monstrosity of peroxidase granules). But as for the qualitative monstrosity, my own case seems to be the very first one in the world literature.

As described already, the present case had xerodermia pigmentosum, albinismus fundi oculi utrisque and albinism of hair. So the question that there might be some hereditary relation between the present abnormity of peroxidase granule of leucocytes on one side and pigmentary changes of skin, hair and eye-ground was raised. Then three cases of xerodermia pigmentosum, two cases of retinitis pigmentosa and one case of total albinism were subsequently examined, but there was no abnormity of the peroxidase granules of leucocytes in any of these cases. Consequently, it should be concluded that the simultaneous occurrence of xerodermia pigmentosum and albinism of ocular fundi and hair in this case was probably an accidental coincidence, and an unrecognized factor, which is responsible for the occurrence of G.P.G., was independent of the known factors responsible for above quoted pigmentary changes.

Although the present case showed a considerable similarity to a case of acute leukemia of leucopenic type (Cf. Anemia, splenohapatomegaly, lymphadenopathia, hemorrhagic diathesis and acute fatal course.), it will be easy to distinguish the latter condition, for it is associated with a distinct predominance of a single type of cell in the bone marrow or/and in the blood in leukemic cases.

What was striking especially in the present case was the large number of G.P.G., the obvious aggregation of fine peroxidase blue granules producing gigantic clumpy effects in leucocytes. There has been no reported case of any known blood dyscrasia that showed such a monstrous abnormity of peroxidase granules. I am quite unable to account for this monstrous abnormity of peroxidase granules on any other basis than a congenital chromosomal defect which might have been due to intermarriage.

The function of peroxidase in the leucocyte has as yet not been investigated in detail. According to Agner[4] the verdoperoxidase occurs in high concentration in the leucocytes. It would seem strange if this high content of verdoperoxidase were needed merely for the oxidative conversion in the leucocytes. It is conceivable that it also has a function in connection with the general reaction of the leucocytes to infection and similar states. One function of it is connected with the hematopoiesis, I believe it on the basis of " Peroxidase Response[5] " which I described already in this Journal. In the present case an abnormal or rather monstrous arrangement of peroxidase granules in the leucocytes (which were themselves abnormal) might have a close connection with a short span of life of such a patient.

Notes

1) It is to be noted here that the mother's blood did not show any abnormity of the peroxidase picture. The father failed to come to our Department in spite of our repeated request.

2) It is a great regret that I did not apply my own method of counting chamber method[7] of peroxidase reaction, by means of which a possible abnormity of the erythron might have been revealed. As has already been described in supravital method (Cf. III), some erythrocytes showed abnormal pictures and one erythroblast even a peroxidase abnormity. If I shall ever come across a second case of the disease, I shall make a point of studying the erythrocyte peroxidase by this method.

Summary

1. In this paper the first case ever reported of qualitative abnormity of peroxidase of blood leucocytes was outlined and the name of " Congenital Gigantism of Peroxidase Granules " was suggested for this abnormity.

2. The Congenital Gigantism of Peroxidase Granules represents a monstrous malformation of the peroxidase granules—obvious aggregation of fine peroxidase blue granules producing gigantic clumpy effects in each cell—of all the myeloic leucocytes in the blood or/and bone marrow (Fig. 3, Fig. 4 and Fig. 5).

3. The Giemsa stained picture of the blood or/and marrow smears of this case was also in no way normal, while the morphological change was not always corresponding to the abnormal peroxidase granules (Cf. Fig. 6 and Fig. 7).

4. The oxidase granules of blood and marrow cells of this case showed a monstrous malformation similar to those of peroxidase granules. So the name of " Congenital Gigantism of Oxidase Granules " may be used instead.

5. The supravital method revealed a peculiar behavior of neutral red vacuoles in neutrophils, monocytes, lymphocytes and red blood corpuslces (Cf. Fig. 8).

6. This patient had photophobia, xerodermia pigmentosum, albinismus fundi oculi utrisque and albinism of hair. He died at 11 months of age developing, besides bronchopneumonia, hepatosplenomegaly, jaundice, melena and pancytopenia.

7. The family pedigree of this patient is characteristic. The parents were of consanguinous marriage. Three sibs had the same congenital stigmata i.e. photophobia, pale color of hair, pigmentation of uncovered parts of the skin and died very early in life during some infection in the

clinical conditions very similar to the present case. It is not difficult to suppose that these sibs had " Congenital Gigantism of Peroxidase Granules."

8. The Congenital Gigantism of Peroxidase Granules might have a close connection with a short span of life of the patient.

Conclusions

A case with photophobia, xerodermia pigmentosum-like pigmentation of the skin, albinismus fundi oculi utrisque, albinism of hair and pancytopenia was presented in the present paper. The most characteristic feature is congenital gigantism of peroxidase granules in myeloid leucocytes. It is a very fatal disease. The name of " Congenital Gigan tism of Peroxidase Granules " is suggested for this new clinical entity.

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References

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5) Higashi, Tohoku J. Exp. Med., 1952, **56**, 330; 1953, **58**, 327.

6) Sato & Hayashi, *ditto*, 1947, **49**, 37.

7) Higashi, ditto, 1953, **57**, 367.

8) Sato, the Quantative and Qualitative Monstrosity of Peroxidase Reaction, to be published in a coming issue of this Journal.