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A STUDY OF 240 CASES OF HAEMORRHAGIC SMALLPOX

by

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INTRODUCTION

It has long been recognised that the Haemorrhagic variety of smallpox differs in several respects - epidemiological, clinical etc. - from the non-haemorrhagic varieties. Of course, as regards the prognosis, this is the most fatal variety of smallpox. However, it is definite, (I think, from the evidence available,) that this variety is not caused by any different strain of virus of variola major. In a majority of instances, whenever the source of infection could be traced, a non-haemorrhagic case was the source for the haemorrhagic and similarly it is not uncommon to find a haemorrhagic case producing a non-haemorrhagic variety in a close contact. Why only certain people should develop this particular fatal variety is not clearly understood at present. But it looks as though it is not mere want of immunity that is responsible for the occurrence of this variety; there must be some other factors playing a role in this. I propose in this paper to present only some epidemiological and clinical data from a study of 240 cases of haemorrhagic smallpox which will show that there is something which we do not know that is responsible for the occurrence of this variety, and that this particular variety differs from others in several respects.

Curshman (1875) described this condition and has divided this variety into two types viz. "Purpura Variola" and "Variola Haemorrhagica Pustulosa". Some authors doubt whether these two types are distinct from one another, or the

difference is only a degree of severity. Ricketts & Byles (1909) said this classification is "arbitrary". On the other hand Dixon (1962) does not even recognise the word "haemorrhagic" since according to him "while haemorrhages are features of many types, particularly of the fatal cases, they may also be present in quite mild cases and so have no unqualified prognostic significance". However, from the experience I have had during the last 20 years after having seen nearly 25,000 cases of smallpox, I still feel that haemorrhagic smallpox is a separate entity and should be recognised as such.

MATERIAL

The material collected for this paper was from amongst 10,857 cases of smallpox of all varieties admitted to the Infectious Diseases Hospital, Madras during 55 months ending November 1963. Of these, 240 belonged to the haemorrhagic variety.

METHODS OF PRESENTATION

The data about the monthly incidence of smallpox in general and the haemorrhagic variety, the incidence of haemorrhagic variety with reference to the two types, age, sex and vaccinal status are presented. The relationship between pregnancy status and haemorrhagic smallpox incidence is discussed.

Some of the clinical data about the cases of this variety are also described.

Before presenting the data about these cases it is necessary that I should define certain words that are used in this paper.

1. Haemorrhagic Smallpox - Cases of smallpox where haemorrhages occur either into the skin or mucous membranes, or into the skin and mucous membranes are considered as haemorrhagic smallpox.

N.B. Haemorrhages occurring into the base of lesions by itself is not a criterion for inclusion into the haemorrhagic variety unless it is associated with haemorrhage into skin and/or mucous membranes.

2. Haemorrhagic Early - Cases of smallpox where haemorrhages precede the onset of focal rash belong to this type which is also termed Type I smallpox. In some cases focal lesions may not be apparently visible even.
3. Haemorrhagic Late - Cases of smallpox where haemorrhages follow the onset of focal rash belong to this Type which is also termed as Type 2 smallpox. Haemorrhages may occur at any stage of the rash.
4. Unvaccinated -
 - i. Those who were never vaccinated
 - ii. Who were said to have been vaccinated but no evidence of scars of vaccination is seen
 - iii. Who were vaccinated for the first time during the incubation period of the attack (i.e. 12 to 14 days before the onset of fever).
5. Vaccinated - Those who have evidence of marks of vaccination done at one time or other during their lifetime (except those under 4 (iii) above).

ANALYSIS OF CASES

EPIDEMIOLOGICAL DATA

- a) General Incidence: Of the 10,857 cases of all types of smallpox that were admitted during the period of 55 months beginning from 1 May 1959, 240 belonged to the haemorrhagic variety with an overall incidence of 2.2%. Of 240, 41.7% belonged to Type 1 (100) and the remaining to Type 2 (140).
- b) Annual Incidence: The annual incidence is not quite consistent. The percentage incidence varies from 1.6 to 2.7 and it cannot be said that it is more in the epidemic years.
- c) Monthly Incidence: Here again, it has not got much consistency. The proportionate incidence to the total smallpox varies from month to month, with a maximum of 3.4% in February to a minimum of 1.6% in September. It has no

relationship even to the total cases of smallpox occurring in each month. For instance, the maximum monthly mean number of cases of smallpox was 367 in March and minimum monthly mean was 101 in November, but the maximum and minimum mean figures for haemorrhagic smallpox were 9.5 in February and 3.0 in May and June (vide Statement 1).

- d) Incidence and Sex: 72% of type 1, and 55% of type 2, were females irrespective of age and vaccinal status. It is more predominant in females especially in type 1.
- e) Incidence, Age and Sex: Irrespective of vaccinal status, 96% of females and 71% of males of Type 1 and 84% females and 78% of males in type 2, were amongst adults over the age of 15 years.
- f) Incidence with reference to Age, Sex and Vaccinal Status

In general, the proportion of the unvaccinated to the vaccinated was 2:3 in type 1, and 1:1 in Type 2. 100% of females and 90% of males in the vaccinated, and 8% of females and 59% of males in the unvaccinated, belonged to the group of adults over 15 years in type 1.

97% of females and 87.5% of males in the vaccinated, and 68% of females and 63% of males in the unvaccinated, belonged to adults above 15 years in type 2.

- g) Haemorrhagic smallpox and pregnancy status: During the period under study, there were 323 pregnant women with smallpox with an overall incidence rate of about 3.0%. The proportionate incidence of the pregnant to the total in each month is maximum in February just like haemorrhagic smallpox.

Taking the age group 15-45 years as the susceptible age group for pregnancy with haemorrhagic smallpox to total haemorrhagic smallpox against women in that age group, 67% of vaccinated and 61% of unvaccinated in type 1, and 23% of vaccinated and 21% unvaccinated in type 2 were pregnant.

Statement 2 shows the incidence of haemorrhagic smallpox with reference to the two types, age, sex, vaccinal status as well as the number of pregnant cases in them.

CLINICAL DATA

The clinical features of haemorrhagic smallpox are well known. Especially in type 1, prodromal symptoms are very severe and prolonged, and the cases may die even before the exanthem is frankly seen. The high toxicity, severe headache, excruciating backache, heaviness in the chest, flushed appearance of the whole body, anxious and pale look, restlessness and appearance of a few abortive papules here and there on third or fourth day of fever, the velvety touch and colour in late stages, consciousness of the impending death and the sudden end are characteristic of type 1.

In type 2, the prodromata may or may not be severe, but the constitutional symptoms will drag on, even after the onset of exanthem, and in the majority of cases the lesions show haemorrhages into their bases and flatten out with haemorrhages appearing into the various mucous membranes. Evolution of rash usually stops and the case becomes more and more toxic. Statement 3 shows the incidence of various types of bleeding that are met with in the two types of haemorrhagic smallpox.

PROGNOSIS

Type 1 was 100% fatal. None survived. In type 2, there were 11 survivals out of 140, with CFR of 92%. There were more survivals in the vaccinated than in the unvaccinated. The mean day of death in type 1 was 5.95 and in type 2 was 10.2.

DISCUSSION

In general, about 1% of the total cases are haemorrhagic early and a little more than 1% are haemorrhagic late. There does not seem to be much consistency either in the annual or monthly incidence, though usually, the highest incidence of this variety is in the month of February.

Both types are more common in the female sex, especially the type 1. For all types of smallpox, the incidence with reference to sex is almost the same, whereas in smallpox type 1, 72% of the cases are females and in type 2 they number 55%.

With reference to age, it is a disease mostly of adults. It is far more common in adults over 15 years especially type 1. When this is compared to all types this will be well appreciated. In the unvaccinated, both in males and females, only 14.15% are adults over the age of 10 years. The corresponding figure for the type 1 is 77.5%. In the vaccinated for all varieties of smallpox, 90% of the cases are over 10 years and the corresponding figure for type 1 is 93.5%. Even in the unvaccinated, if the want of immunity is the reason for this variety, one would expect greater incidence in children under 10 years as is the case with non-haemorrhagic, but it is not so. This is important evidence to show that it is not the want of immunity that is responsible for the occurrence of this variety but something else.

As regards the association of pregnancy and haemorrhagic smallpox, it is not sheer coincidence that 66% of type 1 and 35% of type 2 cases between ages 15-45 years were pregnant because we have shown in another study that the incidence of pregnancy was a little less than 20% in the non-haemorrhagic variety of smallpox of the same age group, 15-45 years. It was also shown in that paper that in all cases in the age group 15-45, the incidence of haemorrhagic smallpox is roughly in the proportion of 2:4:15 respectively in males, non-pregnant females and the pregnant. This shows not only that more than half haemorrhagic cases in females occur amongst pregnant women, but the pregnant stands nearly seven times greater risk of getting haemorrhagic variety when compared to a man of similar age group. Thus there seems to be some host factor which is present mostly in adults especially females and pregnant females, which may at least partly explain the cause of occurrence of haemorrhagic smallpox.

CONCLUSION

There does not seem to be any doubt that the haemorrhagic variety as such is quite different from the non-haemorrhagic varieties of smallpox, both epidemiologically as well as clinically. I do not think it is fair to say that it is simply a severe variety of smallpox because:-

1. like other severe varieties it does not occur mostly in the unvaccinated

2. it is far more common in females
3. it is far more common in adults than in children
not only in the vaccinated but even in the unvaccinated.
4. it is invariably fatal. Even in the vaccinated where
the C.F.R. is only 2-3% in the non-haemorrhagic,
haemorrhagic is 100% fatal.

These definitely indicate that the etiological and epidemiological factors for the occurrence of this particular variety, if the strain of the virus is the same, lie in the particular host. This requires further elucidation. The fact that pregnant females are more susceptible to this fatal variety may indicate that there may be some hormonal factor playing a role.

As regards the type 2, whether it differs from type 1 only in the degree of severity or it is a different entity cannot be said for definite. One thing seems to be certain; haemorrhages occurring in smallpox cases have prognostic significance and haemorrhagic late has more common features with haemorrhagic early than with non-haemorrhagic, both epidemiologically as well as clinically, and so it should be classified under haemorrhagic variety.

SUMMARY

1. Epidemiological and clinical data of 240 consecutive admissions of haemorrhagic smallpox cases into I.D. Hospital between May 1 1959 and November 30 1963 are presented.
2. The overall incidence is about 2.2% of the total smallpox admissions and the proportionate incidence varies from month to month with a maximum in February and minimum in May and June.
3. Two types of this variety are described, haemorrhagic early and haemorrhagic late.
4. Both types are more common in females.
5. The disease mostly occurs in adults.

6. Vaccination does not seem to offer the same protection as it does for the non-haemorrhagic varieties since it is quite common in the vaccinated and is rather rare in the unvaccinated children under 5 years.

7. The pregnant seem to have special predilection for this variety.

8. Type 1 is 100% fatal; type 2 92% fatal.

9. Arguments were put forward to show that haemorrhagic variety is a definite clinical entity different from the non-haemorrhagic type, and there may be some host factor peculiar to adults, especially the pregnant women, which may be playing a role in the etiology of the variety.

10. It is suggested that there may be some hormonal disturbance in certain persons which is responsible for the occurrence of this variety.

TABLE I
showing the incidence of all types of smallpox,
haemorrhagic smallpox and pregnant with smallpox monthly variations

CONTINUATION

Year	January	February	March	April	May	June	July	August	September	October	November	December	Total		
1959	4	4	5	5	5	6	6	6	7	7	7	7	7	1316	
1960	164	247	227	208	116	147	147	154	168	171	175	175	175	2177	
1961	201	423	655	621	391	336	314	190	139	93	52	152	3666	36	
1962	11	6	21	19	18	12	10	8	7	21	14	6	2	1	123
1963	10	7	14	5	10	3	4	9	11	2	4	5	2	4	129
TOTAL	31	22	47	38	38	26	22	27	27	15	33	15	19	19	1462
Monthly Mean	7.75	5.5	11.75	9.5	9.5	6.5	5.5	6.8	5.4	3.0	6.0	3.0	6.6	6.6	36
Percent Proportionate Incidence of Haemorrhagic Smallpox to Total	2.8	3.4	2.1	2.5	1.7	2.0	1.8	2.2	1.6	1.6	1.8	2.4	2.1	2.2	48
Percent Proportionate Incidence of Pregnant with Smallpox to Total Smallpox	3.9	4.2	3.0	2.0	2.1	4.3	3.0	2.0	2.8	3.2	2.0	1.4	1.4	3.0	323

Figures under this column = Pregnant with smallpox
= Haemorrhagic smallpox.

STATEMENT 2 - Since the bacteriological smallpox cases with reference to the 1950-51 medical statistics, age and sex, the segment and survivals are also shown.

TABLE 2

Age	Vaccines	HOSPITALISATION RATE			TOTAL			VACCINES			TOTAL			VACCINES			TOTAL		
		Un-	Vacc.	Total	Un-	Vacc.	Total	Un-	Vacc.	Total	Un-	Vacc.	Total	Un-	Vacc.	Total	Un-	Vacc.	Total
Below 1-37.	1	-	1	-	-	2	1	2	1	2	1	2	1	1	2	3	1	2	3
1-5	4	2	5	2	2	5	2	7	6	7	4	7	1	6	11	1	12	12	
6-10	2	1	1	1	3	1*	3	2	1*	5	4	1*	7	3	1*	10	1	2	
11-15	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	
16-20	3	3	3	28	10	9	13	11	3	13	16	3	3	6	1*	10	8	16	
21-25	6	4	10	8	6&	16	15	24	18	14	20	34	5	1*	8	11	3*	32	
26-30	2	3	5	3	28	12	8	15	18	5	25	20	1*	4	1*	8	14	16	
31-35	2	2	2	3	18	9	5	32	6	5	9	24	2	4	5	1*	3	10	
36-40																			
41-45																			
46-50																			
51-55																			
56 & over																			
Total	17	16	23	23	118	49	33	12	44	40	60	100	21	25	32	5	35	140	

* Survivors

** Pregnant

Showing types of boundaries in the two types of cases.