Rubella Retinopathy

An account of six cases

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The pigmentary retinopathy which may follow prenatal rubella is not rare and has been well documented in the ophthalmological literature. Gregg attributed the first observation of it to Aileen Mitchell who, in 1939, reported a case of left monocular cataract and stated 'the fundus of the right eye appeared pale and some scattered irregular spots of pigment were observed' (Gregg, 1941; 1946). The early Australian reports were followed by others from the U.S.A., South America, and Europe (Reese, 1944; Ramon-Guerra, 1955; Franceschetti and Bourquin, 1946). Thus, within five years of Gregg's original description of the rubella syndrome, the retinal lesion was well known to ophthalmologists. It is, however, still not widely known among paediatricians and was not mentioned among a variety of minor abnormalities in the Ministry of Health's large prospective study of children born following pregnancy complicated by

rubella in the first 16 weeks (Sheridan, 1964). Nevertheless, without a special search, six cases have been encountered in less than a year in the Neurological Unit of the Royal Hospital for Sick Children, Edinburgh. Since recognition of rubella retinopathy may be of diagnostic and prognostic value, it seemed worth while drawing attention to it, and to this end these cases will be outlined and the condition discussed.

Clinical Findings

From Table I which summarizes the case histories of patients it can be seen that in Cases 1, 2, 3, and 4, the maternal illness was diagnosed at the time as typical rubella. In Case 5, the occurrence of cataract and in Case 6, deafness, suggested that in these, too, the mother had suffered from rubella rather than measles.

The typical appearance which we have seen and which is recorded in the literature is illustrated in Fig. 1. There is abnormal pigmentation concentrated at the posterior pole of the eye and consisting of sprinkled dust-like black particles interspersed with larger dots and

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TABZ
Summary

Case No.	Sex and Age (yr.)	Family History of Congenital Malformations	Pregnancy	Labour and Delivery	Birth Weight (kg.)
1	F 4½	None	Rubella 9th week, despite γ-globulin 5 days after exposure	Normal	2.4
2	F 2½	Mother had previous miscarriage, stillborn hydrocephalic and infant with Hirschsprung's disease; mother's sister mentally defective	Rubella at 9 weeks	Normal	2.4
3	M 2½	None	Rubella 4th month	Normal	3.0
4	M 7	Mongol sib	Rubella 8th week	Low forceps	4.0
5	M 1½	None	Rubella or measles at end of 1st month; influenza 2 weeks later	Normal	3.0
6	M 7½	None	Measles or rubella 3rd month	Normal	3.0

specks. Towards the periphery, the deposits become finer and fade out. The pigmentation rarely involves the periphery or assumes the bone spicule formation typical of hereditary retinitis pigmentosa. Histologically, the cells of the pigment epithelium are irregular in size and shape; many of the pigment granules have been shed and those that remain are displaced towards the inner portion of the cell (Ballantyne and Michaelson, 1962). Although Duke Elder (1964) states that rubella retinopathy is always bilateral, unilateral cases have been described (Blankstein and Feiman, 1952), and, as in Case 3, the eyes may be affected very asymmetrically.

Formal testing of visual acuity was not possible in all the patients described, but their vision was, for practical purposes, normal and showed no signs of deterioration. Good vision and the absence of optic atrophy are characteristic of almost all reported cases, and Hogan (1958) was exceptional in believing that vision was almost invariably reduced.

Discussion

The finding of this pigmentary retinopathy which is a common component of the rubella syndrome may shed light on the aetiology of associated congenital malformations if there is no history of maternal rubella, or if, as is not infrequent, the history is of a nondescript illness or skin rash in early pregnancy. The appearance and central distribution of the lesion are sufficiently characteristic to distinguish it from retinitis pigmentosa which may also be associated with deafness and neurological lesions and in which the prognosis for vision is poor. The presence of atrophy of the iris stroma, though not seen in our cases, may confirm the diagnosis of rubella retinopathy (Emerson, 1958).

The high incidence of neurological disorders in

FIG. 1.—Typical rubella retinopathy. (Reproduced by kind permission of the publishers of *Ophthalmologica*.) (Franceschetti, Dieterle, and Schwarz, 1958).

the patients described here is probably the result of selection and has not been described in other reports of the rubella syndrome with or without retinopathy. By far the most commonly associated lesion is nerve deafness which was present in all but one of our cases, and is outstanding in those reported in the literature (Table II). The pre-eminence of deafness as an associated lesion is arresting, and the fact that it tends to follow infection relatively late in the first trimester (the cochlea first appears in the 7th week) suggests that retinopathy may also result from

Cases

Condition at Birth	Fundi	Lesions Associated With Retinopathy	IQ	EEG
Good	Pigmentation at posterior poles and midzone	Deafness; ataxia	85	Normal
Good	Pigmentation at posterior poles	Deafness; ataxia	Low 70's	Normal
Good	Pigmentation at posterior poles left > right	Deafness	Above average	Normal
Good	Pigmentation at posterior poles and midzone	Deafness; mild diplegia	90-95	Normal
Good	Pigmentation at posterior poles	Bilateral cataracts	Mild developmental retardation at 15 months	Normal (EEG audiometry also normal)
Apnoeic, resuscitated with difficulty	Pigmentation at posterior poles	Deafness; diplegia; mental defect	< 50	Normal

TABLE II
Lesions Reported in Association with Retinopathy

Lesions	No.
(A) Cataract	11
(B) Cataract + congenital heart disease	5
(C) Cataract + congenital heart + deafness	1
(D) Congenital heart disease	1
(E) Congenital heart disease + deafness	1
(F) Deafness	75
	94

comparatively late infection. The majority of reported cases of retinopathy with deafness, however, come from three large ophthalmological surveys of rubella-deafened children in which unfortunately the timing of maternal infection is not stated (Marks, 1946; Hamilton, Phillips, Palfreyman, and Waterworth, 1948; Morlet, 1949). An attempt is made in Fig. 2 to summarize reported cases (including the 6 described) which are adequately documented as regards both the associated lesions and the timing of maternal infection. In the first

month, cataract alone, or accompanied by congenital heart disease, is the main associated lesion, while in the second and third months deafness takes over. It is evident also that these cases of retinopathy are evenly spread over the first three months with respectively 9, 9, and 10 cases in each. The evenness of this distribution over the first three months, which contrasts strikingly with the marked tendency for the incidence of the other lesions to fall off, as shown, for example, by Dekaban, O'Rourke, and Cornman (1958), has embryological implications which call for brief consideration.

Pigment begins to appear in the outer layer of the optic cup at the 7 mm. stage, and has increased considerably by the 10 mm. stage, placing the important period of pigment deposition in the 5th week of embryonic life. This is earlier than the development of even the primary lens fibres, which begin in the 6th week (Mann, 1964). It is, therefore, somewhat surprising that though cataract has only rarely been reported with deafness, the combination of retinopathy and deafness, a relatively late lesion, is common. The possibility arises, therefore, that the rubella virus may act not only by interfering

FIG. 2.—Associated lesions and timing of maternal infection in 28 cases of rubella retinopathy. This figure is based on present cases and the following (Babel and Dieterle, 1960; Beswick, Warner, and Warkany, 1949; Blankstein and Feiman, 1952; Cordes, 1945; Dekaban et al., 1958; Emerson, 1958; Franceschetti and Bourquin, 1946; Francois and Verriest, 1956; Gregersen, 1958; Hopkins, 1949; Ellett, 1945; Long and Danielson, 1945; Swan, Tostevin, Moore, Mayo, and Black, 1943; Swan, Tostevin, and Black, 1946).

with developing pigment epithelium, but at least in some of the later cases by damaging that already formed. In this context, a case described by Lundström and Boström (1958) of irregular fundal pigmentation in a child whose mother had rubella in the 8th month of pregnancy is interesting. Moreover, the retinopathy may occasionally be simulated by retinal changes resulting from postnatal viral infections, including measles (Walsh, 1947) and mumps (Bischler, 1945).

While it is generally true that the lesions found in the rubella syndrome depend on the stage of prenatal development at the time of infection, the resultant malformations are less closely related to the timetable of embryonic development than those following, for example, thalidomide administration. In addition to the possibility suggested above that later infection may damage tissues that have developed earlier, it may be, conversely, that organs that have not even begun to develop at the time of maternal infection are malformed as a result of persistence of the virus in the embryo; this has recently been demonstrated (Kay, Peppercorn, Porterfield, McCarthy, and Taylor-Robinson, 1964). This would explain, for instance, the not unusual cases of deafness following maternal rubella in the first month and cases such as the child described by Dekaban *et al.* (1958), whose mother had rubella in the fourth week of pregnancy and who showed no fewer than 11 congenital abnormalities, including deafness, cataract, heart disease, and retinopathy.

Summary and Conclusions

Six cases of rubella retinopathy seen within a year in a children's hospital are described and the condition is discussed.

Unlike retinitis pigmentosa, rubella retinopathy is not progressive and has little, if any, effect on vision. Its main significance is its ability to 'label' other congenital malformations such as cataract, heart disease, and deafness in the absence of a definite history of maternal rubella. This, and the differential diagnosis from retinitis pigmentosa, make its recognition of importance to paediatricians.

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