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CLINICAL ARTICLES

GROWTH AND BEHAVIOUR OF KELOID TRANSPLANTS

By

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The occurrence of keloid in man is as old as mankind itself, but it was not recognised by the ancients. Alibert (1806) is usually credited with the earliest recognition of this clinical entity, although he used the term 'Cancroid'. Subsequently in 1825, he introduced the modern spelling "Keloid". In the following thirty years there was no significant advance in the appreciation of the true nature of this condition and a confusing terminology prevailed about it in the literature.

Addison in 1854, recognised keloid as a white, small opacity appearing spontaneously in the skin and he called it a true keloid, Addison called Alibert's lesion a 'false keloid', thus differentiation between a true (spontaneous) and false (following trauma) keloid was made. Many publications were concerned with the difference between a true and false keloid, but little constructive assessment of this lesion was made until the work of Cosman and others (1961). All workers in this field recognised one invariable feature of this condition viz-prompt recurrence after removal. A number of explanations have been put forward to account for this peculiar behaviour but no explanation was found to be entirely satisfactory

In 1967, Calnan and Copenhagen published a very interesting paper to show the role of local factors in the production of keloids in the anterior abdominal wall in ten patients and studied the growth and behaviour of both the transplanted keloid and original area from where keloid was excised for three years. They found that most of the keloids recurred in the original area within eight and half months of excision. On the contrary, in nine out of ten cases transplanted keloids established fully and merged with surrounding skin surface looking like full thickness skin grafts.

Encouraged by this work, the present study has been undertaken to develop and investigate this line of thought further.

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Material and Methods: The present study includes thirty cases of keloids who attended the surgical out-patients department of Irwin Hospital, New Delhi, over a period of one year (from 1st August, 1968 to 31st July, 1969). The nature of operation proposed i. e. excision of keloid and transplantation of part of it to the thigh, was explained to all the patients carefully. Some patients declined the treatment and only those 30 cases who accepted this form of treatment and voluntarily offered co-operation have been included

Small keloids, specially of spontaneous origin were selected. All except two cases were operated upon under local anaesthesia, using two per cent lignocaine solution for infiltration. For two children general anaesthesia was employed, because co-operation was considered unlikely under local anaesthesia.

An incision was made around the margin of keloid which was excised along with a part of subcutaneous tissue. Skin margins were undermined to facilitate closure without tension and were then sutured with fine linen using interrupted stitches.

The excised keloid was divided into two parts, One part was retained for histopathological study and fixed in 10 per cent formalin solution. The other part of excised keloid was trimmed to measure 2 cm x 1 cm x 3-4 mm. A piece of skin about 2 cm x 1 cm x 3-4 mm. was now excised from anterolateral aspect of thigh and the keloid prepared for transplantation was sutured into this raw area using interrupted sutures of 4/0 silk (Fig 1). Both the wounds were covered by dry dressing.

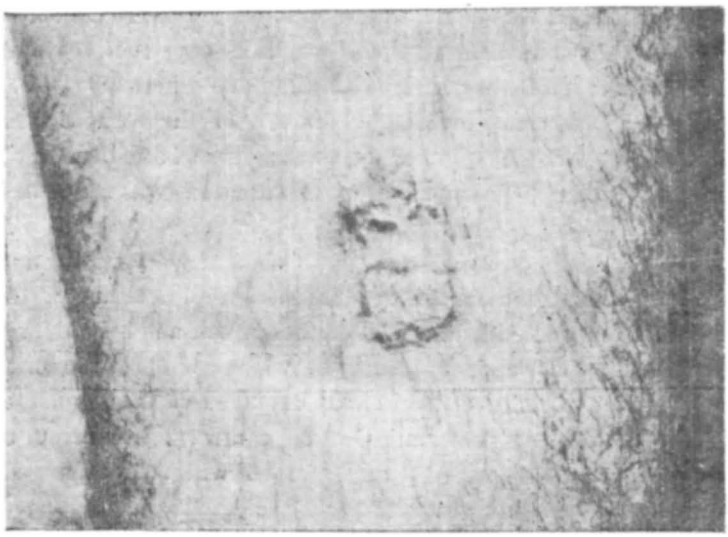

Fig. 1 : A keloid transplant just after operation showing the technique of transplantation.

Post-operative follow-up : On eighth post-operative day sutures were removed and both the wounds were carefully examined.

After the initial visit, cases were followed up fortnightly for first two months, and later at intervals varying from one to three months. At the time of each visit; the original area of keloid and the area in the thigh receiving a keloid transplant, were carefully examined for recurrence, colour changes and compared with the normal surrounding skin of the area. In some cases of recurrence of keloid at the site of excision, a course of radiotherapy was given using a total dose of 1200-1500r in 4 successive sittings. The transplanted keloid was not subjected to radiotherapy in any case.

At the end of maximum follow-up period which varied according to time and date of transplantation (from 2 months to 11 months), a second biopsy was taken from ten cases of successfully established keloid grafts. This was again subjected to histopathological examination to note the changes in structure in transplanted keloids which had regressed in the course of time. The original histo-pathological features were compared with the histology of excised transplants.

Observations and Results: The present study comprises thirty cases of keloids, selected carefully for the purpose of transplantation. For our study we preferred small and idiopathic keloids (24 out of 30 cases). Keloids in both sexes and of all age groups were included. The maximum incidence was between 21-30 years of age (about 36. 7%) and was slightly more common in females (M : F = 43.3:56.7). Keloids on any part of the body were included and their relative distribution is shown in Table I.

TABLE—I :

Anatomical Distribution.

Region	No. of cases	% of Total
Chest	8	26.7
Shoulder	6	20.0
Arm and forearm	4	13.3
Thigh and legs	4	13.3
Head and neck	3	10.0
Back	3	10.0
Abdomen	2	6.7
Total	30	100.0

Chest was the commonest site in our series. Next common site was the shoulder region. Relatively less number of lesions were found on the other regions of the body.

Clinical examination revealed that the epidermis was intact in all cases but it was tense and shiny. Surface was smooth but slightly wavy. Margins were well difined but claw like processes from the edge were seen in all cases, showing that the keloids were active and progressive. Colour of the keloids varied from light brown to deep brown but some were pink.

Treatment offered in all cases was excision of keloid without pre-operative radiotherapy. In cases with recurrence, post-operative radiotherapy was used. Behaviour of both the areas i. e. (a) original area from where keloid was excised and (b) the area of transplantation on the thigh, were noted carefully. The observations are described below:

(a) *Sequence of events in original area* :

1. One week after. On eight day stitches were removed. All healed by primary intention except in nine cases where there was infection. The infected area healed within a week by some local application.

2. One month after operation. In five cases scar became broader, and in one out of these five cases, there was itching suggesting recurrence.

   Subsequently when the patients came for next follow up (two months after operation), definite signs and symptoms of recurrence of keloid were found in another case who came for the first time after removal of stitches.

3. Three months after operation. Only 18 cases out of 30 were available in this period of follow-up *Eleven* out of these 18 patients (including six cases already mentioned) showed signs of recurrence. When reviewed further it was found that another *six* cases had signs of recurrence at the end of six months thus it can be seen that a total of *18* cases out of 30 showed recurrence within six months of the original operation (Table II.)

Table-II : Result of Treatment

	No. of cases	% of Total
Recurrence	18	60.0
No recurrence	11	36 7
Not available for follow-up	1	3.3
Total	30	100.0

(b) *Sequence of events at the site of transplantation*

1. One week after. On eight post-operative day the stitches were removed from the transplants and the area carefully examined for,
   i) Viability of transplants.
   ii) Inflammation and infection.
   iii) Colour of transplants.
   iv) Presence cr absence of sensation.
   v) Presence of features of original keloid.
   vi) Formation of new keloid at the site of transplantation.

It was found that six out of 30 transplants did not survive in the thigh. There was evidence of gross infection which gradually dissolved out the transplants. The wounds healed by granulation tissue witha few dressings. The scar was kept under constant observation for the possible development of keloid at features. None of these cases, however, developed keloid during the entire follow-up period.

In the remaining 24 cases, the transplants established successfully. The viability of the graft was evidenced by–

i) Absence of any reaction at its periphery.
ii) Absence of blackish discoloration.
iii) Firm attachment to underlying sub cut-aneous tissue.

In all cases the transplants were brown in colour like normal free skin grafts. Tactile sensations could not be detected in the transplant in any case at this stage.

2. One month after operation. In all cases of successful transplants (24 out of 30), tense and shiny appearance of original keloid was lost. They become dull brown in colour, and no sign of formation of keloid could be detected. There was no tactile, sensation in the transplant at this stage.

3. Three months after transplantation, only fifteen cases of successful transplants were available for study at this stage. In these cases, the transplants had become softer in consistency and light in colour. Tactile sensation was present at the periphery in all these cases. In three cases, sense of pressure was present in the centre of the transplant, though tactile sensation was absent.

4. Six months after transplantation, only ten cases with successful transplants were available for review at this stage. When examined at this stage the tratsplants were level with and only a little darker than the surrounding skin of the thigh. There was no clinical evidence suggestive of keloid formation in the transplant. The colour of the transplants was now only a little darker than the surrounding skin. In three cases tactile sensation was present all over the graft and growth of hair was seen in the centre of the transplant (Fig. 2).

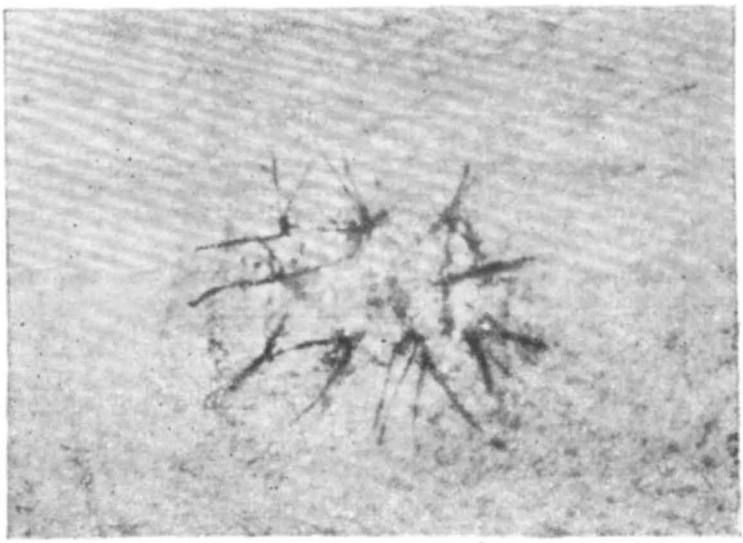

Fig. 2: Keloid transplant seen 6 months after transplantation. Size is diminished. Growth of hair is obvious. Colour approaching towards normality.

Histopathology: Paraffin sections from all the cases were cut at 6 microns and stained by haematoxylin and eosin. Masson's trichrome, Van Gieson, Periodic acid-schiff (PAS), Alcian blue stains were also used when required For purposes of clarify, histopathological findings in the original lesions and transplants are described separately.

(A) ORIGINAL KELOID

Epidermis covering the bulk of keloid is thickened, the dermal appendages are flattened, and a zone varying in width separates the epidermis and the superficial dermis from the underlying keloid.

A keloid is made of thick, glassy, collagen fibres arranged in nodules which merge into each other imperceptibly. In between the nodules, fibres are arranged in an irregular manner (Fig 3). A considerble amount of bluish intercellular substance is present.

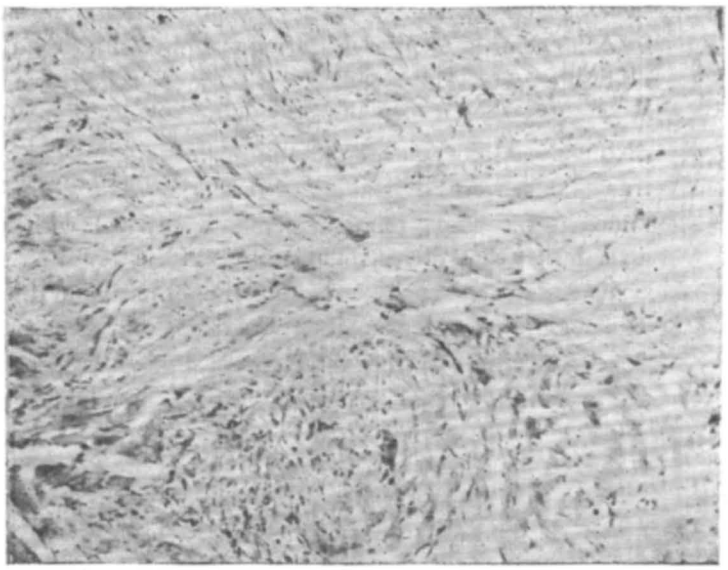

Fig. 3: Showing nodularity of keloid Collagen fibres are arranged in nodules giving a whorl appearance. In between the nodules, fibres are arranged irregularly. The fibroblasts are numerous with abundant cytoplasm and plump nuclai. (Haematoxylin, eosin x 120 – low power).

It is a cellular lesion, showing a fairly large number of cells with plump, oval, and elongated nuclei arranged along the fibres. Little or no chronic inflammatory cells are present. It is thus clear that certain criteria can be laid down for the diagnosis of keloid. They are:

1. Special features and arrangement of collagen fibres.
2. Cellularity of lesion.
3. Absence of chronic inflammatory cells.

When the above criteria were applied to the excised specimens, it was found that only twenty specimens out of thirty could be labelled as true keloids. The remaining ten cases were categorised either as hypertrophic scar (4 cases) or as an

indeterminable group (6 cases). Clinically, however, the last two groups of cases could not be distinguished from keloid by any means.

(B) EXCISED TRANSPLANTS

Ten of the transplanted keloids were excised at intervals varying from 4 to 7 months after operation. On review of histology it was found that in five cases transplants were obtained from true keloids, in four cases from indeterminate group and in one case from a hypertrophic scar.

Some very interesting and striking changes were observed when the histology of excised transplant was compared to that of the piece of keloid from which the transplant was originally obtained. There was a progressive loss of arrangement of collagen bundles so prominently seen in a keloid. A section obtained from a transplant four months after transplantation showed the nodularity is still in existence but less marked than original specimen. The collagen fibres appeared less swollen and glassy and are distinctly laid out. These changes are more marked in the section of a transplant which was excised 7 months after transplatation (Fig 4). Similar changes were also observed in transplants of three other cases where clinically we could detect the growth of hair in them.

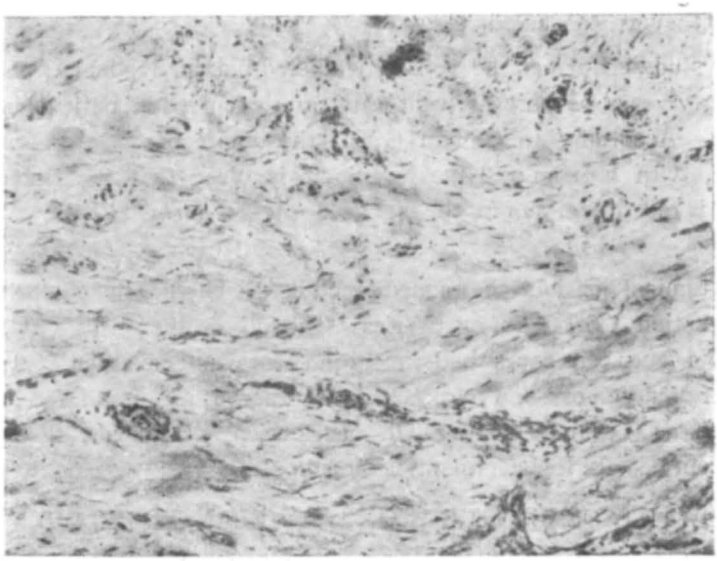

Fig. 4 : Section of the transplant 7 months after transplantation. Fibres are not arranged in nodular fashion and are distinctly laid out as compared with Fig. 3. They are not glassy. Fibroblasts are few with scanty cytoplasm and small nuclei. (Haematoxylin, esoin x 120 - low power).

There was also evidence of progressive reduction in the number of fibroblasts seen in sections. These not only decrease in numbers but also become thinner, flatter with decrease in the amount of cyto-plasm and size of the nucleus, thus resembling more closely the fibroblasts seen in normal skin. Though it is not possible to label the change in any one slide as extraordinary, it was clear

from an examination of transplants of keloids and cases in the indeterminate group that the following two changes take place progressively in the transplanted skin.

1. Loss of nodular arrangement and abnormal character of collagen fibres.
2. A decrease in the number of fibroblasts and a change in their character, so that they approxymate the fibroblasts of normal skin in course of time

DISCUSSION

The exact etiology of the keloid is unknown. A vigorous effort has been made by various investigators to evaluate the various etiological factors responsible for their growth and development.

A new line of thought in this field was provided by Calnan and Copenhagen (1967) by doing autotransplantation of keloid in man to study the growth and behaviour of transplanted keloid. The present study in an attempt to develop and investigate the above line of thought and to establish the role of local factors in the production of keloids.

Thirty cases were included in our study which yielded certain interesting results and they are discussed below.

Our study confirmed the generally quoted maxim age incidence as between ten and thirty years, seventy per cent the cases occurred in patients in the above age group. According to Calnan (1963) the commonest age group is between 8–38 years, with a mean of 22 years. So it is clear that incidence of keloid formation is most common in the age groups when *hormonal* stimulation is high in both sexes.

Anatomical distribution–As mentioned before chest is the commonest site of keloid formation (26.7%) in our series. Though in the series of Cosman et al (1961) only 4.7 per cent cases had keloid in chest where as about 71.0 per cent of lesions were on the head and neck area. So there is a gross difference between these series as regards anatomical distribution of keloids, though in both series, extremities are less commonly affected.

GROWTH & DEVELOPMENT OF TRANSPLANTED KELOID.

Out of thirty cases in the present series, as many as 24 (80.0%) transplants established fully on the thigh. In the remaining six (20.0%) cases the transplant sloughed out completely leaving a raw area which healed by scarring. The most important cause of failure was infection. The infection caused vascular thrombosis resulting in the death of the transplant which became gangrenous and ultimately sloughed off. To achieve a successful transplant, sufficient nourishment (Vascular recipient bed), primary tissue contact, control of bleeding and absence of infection are necessary (Orentreich, 1959). Failure of the transplants may be to any of these causes.

In the series of Calnan and Copenhagen (1967), only one transplant out of ten (10.0%) did not establish. The explanation put forward by them was that the graft was thicker than usual (about 5 mm.). The percentage of falure in our series is definitely higher (20.0%) than that of Calnan and Copenhagen (10.0%).

None of the six cases of unsuccessful transplants in the present series, showed any sign of new keloid formation at the site of transplantation even in the presence of infection and operative trauma which are known to lead to keloid formation. On the contrary, in the series of Calnan and Copenhagen, a new keloid was formed at the site of transplantation in the only case of unsuccessful transplantation (Table III).

Table III : Results of Transplantation

	PRESENT SERIES			CALNAN & COPENHAGEN SERIES (1967)		
	No. of cases	Regression	Recurrence	No. of cases	Regression	Recurrence
Successful transplants	24	24	0	9	9	0
Unsuccesful transplants	6	0	0	1	0	1
Total	30	24	0	10	9	1

The results of successful transplants in the present series correspond with that of Calnan and Copenhagen. They all became paler, soft and flatter within this limited follow up period. The size of the transplant did not alter in most of the cases excepting in three where significant diminution in size was seen within six months of follow up. Besides these, growth of hair was also seen in three of them. In no case, keloid formation was seen in transplanted area or in the transplant itself

Tactile sensation appeared in the periphery within three months in almost all cases and in three cases the entire transplant developed tactile sensation. It is thus seen that a keloid transplant behaves as a free skin graft in almost all respects.

Considering the series of Calnan and Copenhagen, all the successful transplants (90.%) lost their original keloid character and became paler, softer and merged with surrounding skin in the anterior abdominal wall over a follow-up period of three years. In some cases the transplants were so nicely established that the demarcation between the transplants and surrounding normal skin disappeared.

When the changes in the transplants in the present series were reviewed histologically, it was found that out of six cases of unsuccessful transplants, four were originally keloid and two were hypertrophic scars. Among the 24 successful transplants, six were from indeterminate group and two were from hypertrophic scars, remaining 16 transplants were from keloids. The three cases of successful transplants where sensation appeared all over and hair grew in them, are obtained one from each group.

As has been stated already, the transplants were excised from first ten cases at intervals varying from four to seven months after transplantation for comparison of histological study of original lesions and the transplants. In the series of Calnan and Copenhagen (1967), they studied seven cases for histological comparison. The usual sequence in our series, was recurrence of keloids in original area and regression of transplants on the thigh both histologically and clinically.

From the above clinical and histological observations on the behaviour of autotransplanted keloids and the original areas from where the keloids were excised, it is possible to obtain an indirect evidence that keloid is purely a local abnormality. The systemic factors i. e. age, sex familial or hereditary factors etc. are unlikely to be of paramount importance. We included the lesions of all age groups and both sexes but the biological behaviour of transplants or the original areas was not affected in any way irrespective of age groups and sex of the patients. A striking difference in the biological behaviour of the keloids at the site of transplantation and in original area was seen in all cases. This shows that there must be some local factors in the original area which produce keloids there and cause recurrence promptly after excision. Possibly these factors were absent in the thigh as a result of which keloids transplanted in the thigh regressed and keloids did not develop even in the presence of infection and operative trauma.

Our study though limited by a short follow-up period, strongly supports the pioneer work of Calnan and Copenhagen (1967) in this field. It is obvious that local factors play a very important if not an over riding role in the growth, development and recurrence of a keloid. It is neccessary to include a larger number of cases to be followed up over a longer period to reinforce these conclusions.

Summary and Conclusions

1. Keloids from 30 patients were transplanted to a new site on the thigh. 24 of these grafts took completely and these gradually lost all the features of keloid. Six failures produced by infection healed by scarring with no keloid formation.
2. In majority of cases recurrence within a few months followed at the site of excision. These cases were examined repeatedly for several months (up to 7½ months).
3. Histological features of keloids and transplants were examined.
4. The importance of local factors in the development of keloid has been stressed.

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