ORIGINAL ARTICLE

Development of Embryonic Type of Fat in Human Foetal Breast

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Abstract

Adipose tissue is not only regarded as an organ of storage related to fuel metabolism but also an endocrine organ involved in the regulation of insulin sensitivity ,lipids and energy metabolism. Adipogenesis has been studied by different authors taking samples from cheek, chin, periocular fat, inguinal pad fat, epididymal pad fat etc. Very few authors have studied lipogenesis in mammary gland though mammary fat tissue is considered crucial for mammary ductal morphogenesis. So, the development of adipocytes in human fetal mammary gland was studied on forty four foetuses of different gestation period in Government Medical College Jammu. We observed the appearance of preadipocytes at 15th week and organization of mature adipocytes into lobules at 23 weeks of gestation. The morphology of developing adipocytes showed a great variation and a close relationship was observed between adipogenesis and angiogenesis .

Key Words

Foetus, Crown rump length, Pre adipocytes, Adipocytes

Introduction

Adipose tissue is not only regarded as an organ of storage related to fuel metabolism but also an endocrine organ involved in the regulation of insulin sensitivity ,lipids and energy metabolism.(1) Adipogenesis has been studied by different authors taking samples from cheek, chin, periocular fat, inguinal pad fat, epididymal pad fat etc. Very few authors have studied lipogenesis in mammary gland though mammary fat tissue is considered crucial for mammary ductal morphogenesis (2, 3). Mammary gland is a modified and highly specialised sweat gland (4) of mammals which by definition feed their young ones with the milk secreted by such glands (5). The term breast and mammary glands are often accepted as equivalent but they are not strictly synonymous because breast contains tissues (fat, vessels, nerves etc.) other than glandular elements (6) . Some authors Ambazhagan (7) found the association of embryonic fat with the developing ducts during organogenesis of human breast. Most of the study which deals with the development of breast mainly observed changes in the epithelium which form the mammary analage. Very few studies laid stress on the development of mammary mesenchyme of which adipocytes are the major part. The stromal elements develop from the mesenchyme, paripassu with the development of ductal epithelium. It is for this reason that the present study has been undertaken to enable us to study the pattern of adipogenesis in human mammary gland. The formation and maintenance of adipose tissue is essential to many biological processes and when perturbed leads to various diseases (8).Some factors secreted by adipocytes play a key role in promoting the metastatic ability of breast cancer cells(9).So our study would be of help to surgeons, gynaecologists, oncologists etc.

Material Methods

The present study was on carried out on foetuses of

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different gestational periods received from the department of Gynaecology and Obstetrics of Govt. Medical College Jammu. The material was obtained as products of abortions and still births. The collected specimens were put in jars containing 10% formalin. Out of 44 foetuses, 36 were female, 6 were male and sex of 2 foetuses could not be determined. (*Table 2*). The breast bud and surrounding ellipse of nipple containing skin was excised along with underlying soft tissues and kept in a tissue capsule. The specimens after fixation were prepared by paraffin wax embedding method for sectioning. About 6-8 micrometre sections were made in horizontal and longitudinal plane. These were then stained with Haematoxylin and Eosin & Masson's Trichrome stain. The slides were then mounted and observed under microscope.

Results

The present study was carried out on foetuses ranging from 33mm to 270mm crown-rump length. The foetuses were divided into six groups depending on their stage of histological development. (*Table 3*)

Group-1(up to 40mm crown rump length) n=1

There was thickening of the mesenchymal cells in the immediate vicinity of the epidermal thickening which constituted the stromal changes. A few blood vessels were also seen.(*Fig-1*)

Group-2(40mm to 80mm crown-rump length) n=5

The mesenchymal cells near the developing mammary gland had dense and regular arrangement of fine collagen fibres along with fibroblasts. The fibroblasts were seen as cells with oblong oval nucleus. The condensed mesenchymal cells along with fibrils had no definite arrangement. Occasional blood vessels with nucleated red blood corpuscles are seen.(*Fig-2*)

Group-3(80mmto 120 mm crown-rump lengths) n=9

The collagen fibres along with fibroblasts were densely arranged in the form of a horse shoe shaped structure along the developing mammary anlage. Sheets of pre adipocytes were seen around the developing analage of 104mm crown-rump length. The sheets of pre adipocytes were seen in the sub cutaneous tissue below the gland.(*Fig-3*)

Group-4(120mm to 160 mm crown-rump length) n=15

Concentric arrangement of parallel collagen fibres with interspersed fibroblast were seen just adjacent to the mammary gland with sparse arrangement of these structures with capillaries and blood cells. Preadipocytes were seen without characteristics signet ring shape of mature adipocytes with increased number of capillaries and blood vessels. The surrounding connective tissue formed the stroma . The mature adipocytes form groups in the subcutaneous tissue with rich vascular supply showing fibroblasts ,collagen fibres and preadipocytes.(*Fig-4*)

Group-5(160mm - 200mm crown- rump length) n=9

Mature adipocytes were seen along with some preadipocytes. Sub cutaneous tissue showed well developed adipose tissue arranged in the form of well defined lobules showing classic honey comb appearance of adipocytes within these lobules(*Fig-5*)

Group-6(200mm- 270mm crown-rump length) n=5

The sub cutaneous tissue showed a large number of signet ring shaped mature adipocytes along with capillaries and blood vessels arranged in the form of lobules separated by connective tissue septa consisting of collagen fibrils and fibroblast. Few preadipocytes were also seen.(*Fig-6*)

Discussion

There is considerable controversy regarding the histogenesis and cell of origin of pre adipocytes(10) . Light microscopic appearance of the embryonic type of fat at different stages of maturation has been described previously by Ambazhagan *et al* (7).In current study the embryonic type of fat was observed at 15 weeks of gestation. This embryonic fat tissue was composed of developing adipocytes and capillaries which were organised in sheets of round to oval islands surrounded by fibro collagenous tissue. Before 15 weeks only condensation of mesenchyme was seen. The group 2 foetuses also showed some blood vessels with nucleated R.B.C in the condensed mesenchymal tissue. This is in accordance to Wassermann (11) who also described adipose tissue as arising from mesenchymal elements existing in close conjunction with capillaries in primitive adipose organs. Wassermann and J Roth (11,12) have confirmed that fat cells cannot develop without vascularisation. In the present study pre adipocytes appeared at 17 weeks of gestation while fat lobules were formed at 23 weeks of gestation. Our present results were in accordance with Poissonnet C M *et al* (13)who observed differentiation of fat tissue between 14 and 16 weeks of gestation. There is considerable variation in the morphology of the developing adipocytes. These differences were mainly attributed to the different stages of maturation of these cells. A varying number of mature fat cells with eccentric nuclei are seen in the centre of some of these fat lobules. This is in accord with Ambazhagan R. *et. al* (14). The mesenchymal tissue

Table.1 Showing Crown Rump Length

Age of Embryo/Foetus	Crown Rump Length
32 days	5mm
33-55 Days	5mm+1mm per day
56 Days Onward	Calculated Age at 55 days+ one and a half mm per day

Table.2 Showing age and sex wise Crown Rump Length distribution

S. no	CRL(in mm)	Age (in days)	Male/Female	No of cases
1	33	58	-	1
2	43	65	-	1
3	70	83	Female	2
4	77	88	Female	1
5	80	90	Female	1
6	88	95	Female	1
7	90	96	Female	1
8	104	106	Female	1
9	108	108	Female	1
10	110	110	Female	3
11	117	115	Female	2
12	122	118	Female	1
13	125	120	Female	1
14	130	123	Female	2
15	138	128	2Female,1Male	3
16	142	131	Female	2
17	145	133	2Female,1Male	3
18	150	136	Female	2
19	160	143	Female	1
20	165	146	Female	1
21	170	150	Male	1
22	175	153	Female	2
23	180	156	Female	1
24	182	158	Female	1
25	185	160	Female	1
26	190	163	1Female,1Male	2
27	206	174	Male	1
28	210	176	Female	2
29	212	178	Female	1
30	270	216	Male	1

Table.1 Showing Crown Rump Length

Group No.	CRL (in mm)	No of fetuses
1	33	01
2	43 to 80	05
3	88 to 138	16
4	140 to 170	10
5	180 to 200	07
6	206 to 270	05

Fig -1 Showing epidermal thickening (A) and stromal changes with blood vessels (B) in a 33mm CRL fetus H&E X 100

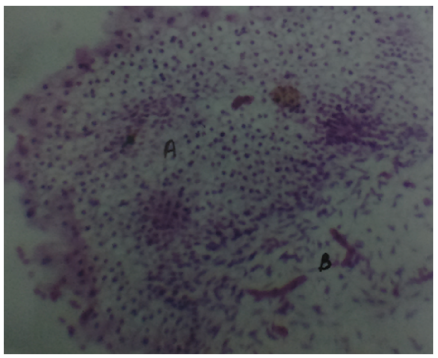


Fig -2 showing mammary pit (A) , neck (B), mammary bud (C) and condensed mesenchyme (D) in 80 mm CRL fetus H&E X 100

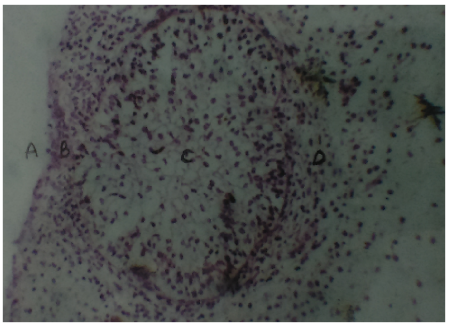


Table.2 Showing adipogenesis and Angiogenesis

Group	Adipogenesis	Angiogenesis
I	Thickening of mesenchymal cells.	A very few blood vessels seen
II	Dense and regular arrangement of mesenchymal cells close to mammary analage and no definite arrangement of mesenchymal cells as we move away	Blood vessels and nucleated RBC seen
III	Sheets of preadipocytes around developing analage	More blood vessels are developing in the surrounding area
IV	Preadipocytes with some mature adipocytes	Rich vascular supply
V	Mature adipocytes in well defined lobules	Rich vascular supply
VI	Honey comb appearance of mature adipocytes with few preadipocytes	Blood vessels are well developed

surrounding the developing anlage forms the stoma of the gland.

Conclusion

Evaluation of the mammary fat pad revealed that pre adipocytes appear at 15 weeks of gestation and fat lobules were formed by 23rd week of gestation, when

Fig -3 Showing fibroblasts (A) ,collagen fibres (B), sheaths of preadipocytes (C) in 104 mm CRL fetus H&E X100

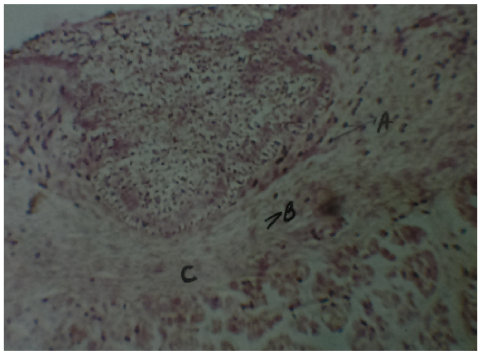


Fig -4 showing preadipocytes (A) and mature adipocytes (B) in 145 mm CRL fetus H&E X 100

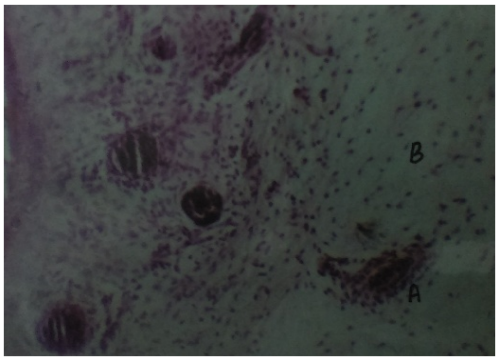


Fig -5 Showing mature adipocytes (A) with blood vessels (B) in subcutaneous tissue (C) in 206 mm CRL fetus H&E X 100

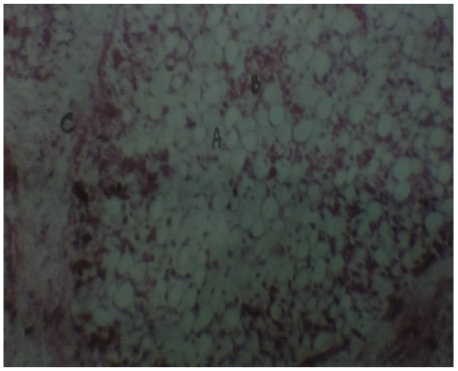
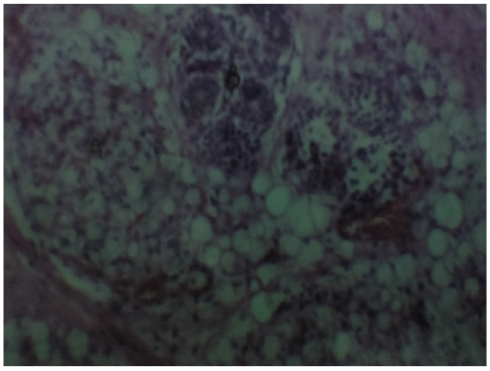


Fig -6 Showing association of lobules of adipocytes (A) with lobules of ducts (B) in 210 mm CRL fetus H&E X 100



each lobule showed a classical honey comb appearance of adipocytes .It was also observed that there was an increase in size of fat lobules with increase in age of gestation, yet their number remained constant after 23rd week. Although only light microscopic observations were made but still we could decipher the relation of prenatal fat development to the development of blood vessels hence conclude that lipogenesis depend on angiogenesis.(*Table-4*).

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