Chapter 14
Hair Disorders in Females

Surabhi Sinha, Meghna Gupta, Shivani Bansal, and Rashmi Sarkar

14.1 Anatomy and Physiology of Hair

The hair follicle is divided into two regions, the upper part consisting of infundibulum and isthmus and the lower part comprising hair bulb and suprabulbar region. Every hair follicle undergoes three phases in its life cycle called anagen (growing phase), catagen (transition phase) and telogen (resting phase). The anagen, catagen and telogen hair comprise 84%, 2% and 14%, respectively, of the total scalp hair [1]. Hair disorders occur due to perturbations in the life cycle of hair or defect in the anatomy and physiology of hair.

14.2 Classification of Hair Disorders in Females

Hair disorders in females are divided into four groups: hair loss (cicatricial/noncicatricial), hair gain (hirsutism/hypertrichosis), hair shaft disorders (with increased fragility/without fragility) and hair pigmentation abnormalities [2] (Fig. 14.1). These disorders can be congenital, autoimmune, infectious or genetic.

S. Sinha (✉)
Senior Specialist & Professor, Department of Dermatology, Venereology and Leprology, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) & Dr. Ram Manohar Lohia Hospital, New Delhi, India

M. Gupta
Department of Dermatology, Venereology and Leprology, G.S. Medical College and Hospital, Pilkhuwa, Uttar Pradesh, India

S. Bansal
Department of Dermatology, AIIMS Bhatinda, Bhatinda, India

R. Sarkar
Department of Dermatology, Lady Hardinge Medical College and Associated SSK and KSC Hospitals, New Delhi, India

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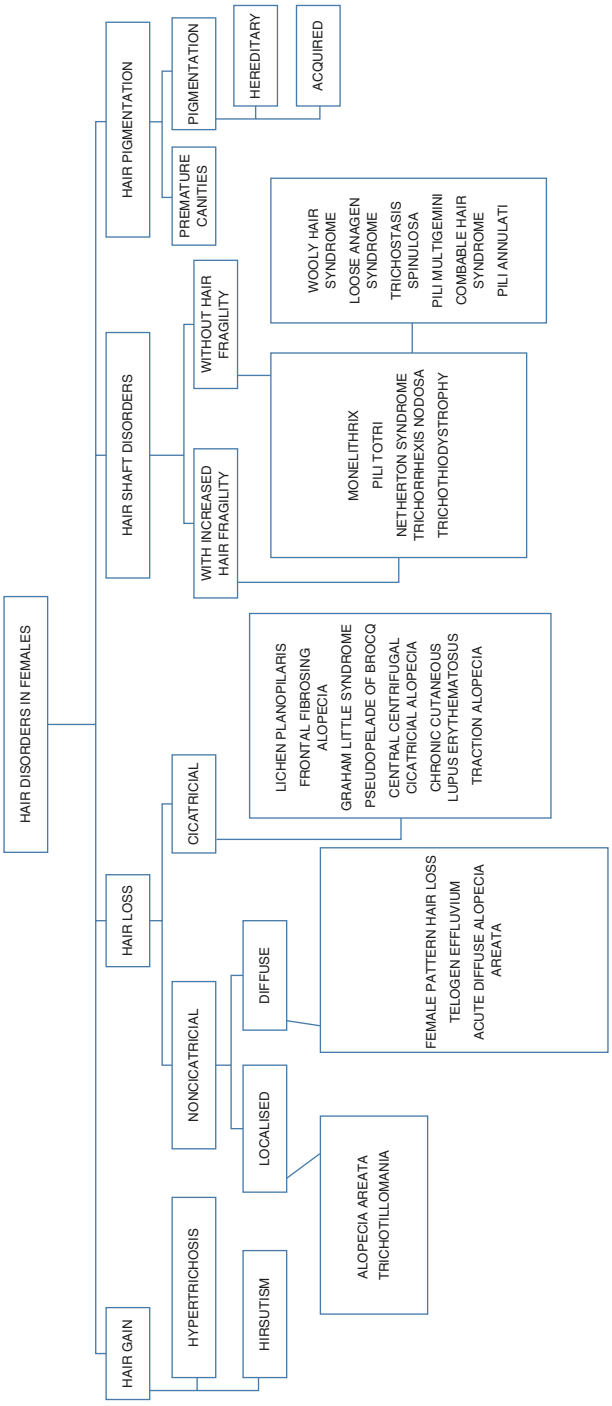

Fig. 14.1 Classification of hair disorders in females

These disorders are discussed in the following sections.

14.2.1 Female Pattern Hair Loss

Female pattern hair loss (FPHL) is the most common type of hair loss in females [3]. Earlier the patterned hair loss in both females and males were collectively called androgenetic alopecia (AGA); however, as there is identification of nonandrogenetic mechanism in its pathogenesis so now the term AGA is limited to patterned hair loss in males and patterned hair loss in females is called female patterned hair loss.

14.2.1.1 Epidemiology

FPHL starts at puberty in females; however, the prevalence increases with age. Twelve percent of women are affected by age 29 years, 25% by age 49 years, 41% by 69 years and >50% have some element of by 79 years in one study [2]. FPHL is commonly seen in Caucasians and has a lower prevalence in Asians.

14.2.1.2 Pathogenesis

The etiopathogenesis of FPHL is complex with multiple factors such as genetics, inflammation, hormones and environment playing a role in it. The pathomechanism behind FPHL is the stimulation of androgen receptors on the dermal papillae of terminal hair follicles by dihydrotestosterone, which leads to miniaturization of the terminal follicle to vellus hair follicle. These pseudo vellus hair follicles have arrector pili muscle attached and angiofibrotic streamers which distinguish them from true vellus hair. There is variation in the size of the hair follicles but the total no of hair follicles remain the same in affected patients. FPHL is more confined to frontal regions and vertex and spares the occipital region because the number of the androgen receptors and DHT enzyme in the hair follicles are more in the frontal region than the occipital region. The severity, prevalence and age of onset of patterned hair loss is less in females as compared to males due to the lower level of 5 alpha-reductase and androgen receptors and increased aromatase content in frontal hair in females. Apart from hormonal factors, various genetic factors also play a contributory role in the development of FPHL. Genes on the X chromosome locus containing the androgen receptor and ectodysplasin A2 receptor have been found to have a role in the early onset FPHL [4]. An Australian Genome-wide association study shows the association of the aromatase gene in the FPHL [5]. Several environmental factors like psychological stress, hypertension diabetes mellitus, smoking, multiple marriages, higher income and little physical activity ae associated with FPHL.

14.2.1.3 Clinical Features

Females can present at initial stages with increased shedding of hair, thinning of hair on the crown or both. Initial cases of FPHL with increased hair shedding are difficult to diagnose. Trichodynia may be associated with FPHL.

There are three different patterns of FPHL:

1. Diffuse thinning of the crown region with preservation of the frontal hairline: there are two scales used for this pattern: the commonly used 3-point Ludwig scale [6] and the 5-point Sinclair scale [7].

Grade	Description
I	Minimal hair thinning on crown which can be camouflaged by hair styling
II	Decreased volume and widening of central partition (more than Grade I)
III	Full baldness in areas of Grade I and II with see through appearance on top of scalp

2. Thinning and widening of the central part of the scalp with breach of frontal hairline, described as the Christmas tree pattern [8]—using the Olsen scale (Figs. 14.2 and 14.3).

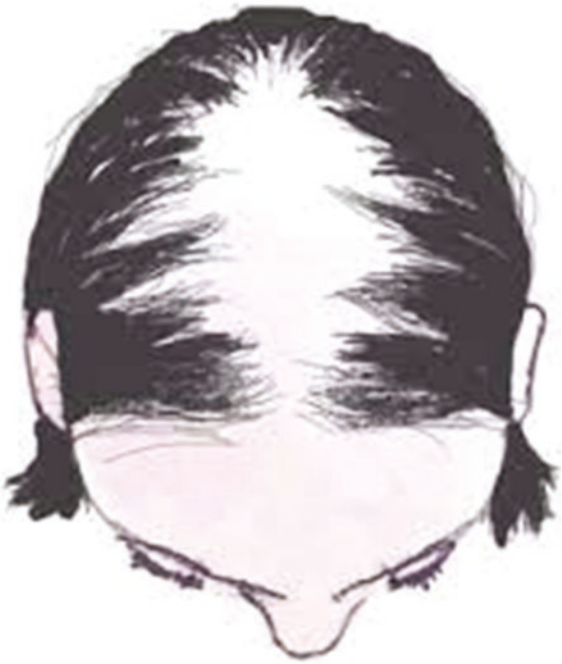

Fig. 14.2 Christmas tree pattern in FPHL

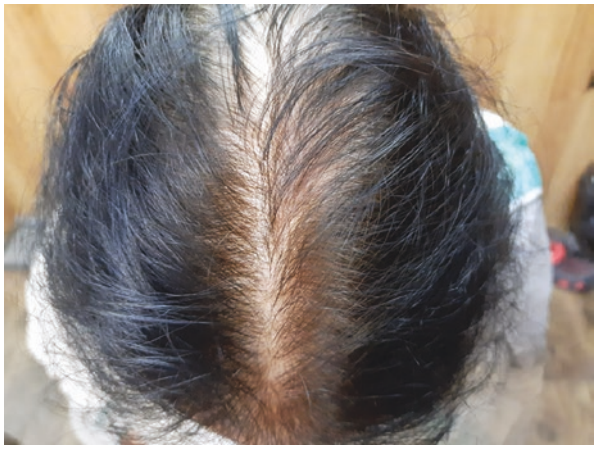

Fig. 14.3 Christmas tree pattern in FPHL

3. Thinning associated with bi-temporal recession; similar to male pattern baldness and classified by the Hamilton–Norwood scale [9].

All these patterns spare the occipital region. However, in some women, the hair thinning can be more diffuse, involving the parietal and occipital areas of the scalp with a pattern of diffuse alopecia.

14.2.1.4 Associations

FPHL has been found to be associated with early cardiovascular disease risk and hypertension due to higher levels of C-reactive protein, higher aldosterone, D-dimers and insulin levels in women [10, 11]. FPHL has been shown to compromise body image and strongly affect self-esteem of patients. In a study, it was found that 88% of females felt FPHL affected their daily life [12].

14.2.1.5 Investigations

The diagnosis of FPHL is usually indicated from a history of a decrease in the girth of the ponytail. Bedside tests like the hair pull test are used to support the diagnosis of FPHL. In hair pull test, 60 hair are held with the thumb and index and middle fingers and pulled upwards and outwards—if more than 10% of the same can be removed, then it is considered to be positive. Hair pull test is positive only in active cases and will be positive in affected regions only unlike telogen effluvium where it would be positive globally. Trichogram can also be used. Dermoscopy can contribute to the diagnosis of FPHL, especially in the early stages of the disease. Histopathology is the most reliable test to differentiate from chronic telogen effluvium Trichoscopic features and histopathological findings helpful in differentiating are given in Table 14.1.

Table 14.1 Diagnostic features of various types of alopecia encountered in female patients

Disease	Clinical features	Trichoscopy	Histopathological findings
Androgenic alopecia	Diffuse thinning on the crown central widening	Hair diameter variability of 20% and terminal hair infundibulum decreased to 1 or 2	Miniaturized hair follicles Terminal to vellus hair ratio <4:1
Telogen effluvium	Sudden onset diffuse shedding of scalp Trichodynia (20%)	Absence of hair fiber variability with large number of regrowing hair	Increased telogen hair >15% Suggestive >25% Diagnostic
Alopecia areata	Well-defined patches of noncicatricial alopecia on scalp, beard	Exclamation mark hair, yellow dots (most common and sensitive, broken hair, black dots and short vellus hair (suggestive of activity and most specific)	*Acute phase*—perifollicular inflammatory infiltrate (*swarm of bees appearance*). The inflammatory infiltrate consists of activated T lymphocytes, macrophages and Langerhans cells. Hair follicles do not progress beyond anagen III–IV *Subacute phase*—Decreased anagen and increased catagen and telogen hair *Chronic phase*—Follicular miniaturization with variable inflammatory infiltrate. Terminal to vellus hair ratio is decreased to 1:1 in contrast to 7:1
Lichen planopilaris	Asymptomatic or present with hair shedding, itching, pain or burning in the scalp Later—develop patches of scarring alopecia with violaceous pigmentation on the surface	Early stage—violaceous background with peripilar scaling at the proximal end of the hair (Figs. 14.4 and 14.5) late stage—shows fibrotic white dot, acquired pili torti, loss of follicular openings, white areas, honeycomb pigmentation, milky red areas and hair tufts	Early stage-band like inflammatory infiltrate and basal cell vacuolation at isthmus and infundibulum Late stage—perifollicular fibrosis with hourglass configuration DIF will show positive staining for colloid bodies, IgM, IgA or C3; linear bands of fibrin or fibrinogen at DEJ

Table 14.1 (continued)

Disease	Clinical features	Trichoscopy	Histopathological findings
Frontal fibrosing alopecia	Progressive recession of frontotemporal line with perifollicular erythema and follicular hyperkeratosis in postmenopausal females	Same as LPP	Same as LPP
Graham little syndrome	Triad of follicular plugins followed by scarring alopecia in the scalp Follicular plugging and noncicatricial alopecia in the axilla and pubis Keratosis pilaris other body sites	Same as LPP	Same as LPP
Discoid lupus erythematosus	Erythematous plaque with follicular plugging which develop scarring alopecia Face and ears can be involved	Follicular keratotic plugs bordered by tortuous blood vessels appearing as red spiders in yellow dots	Early—interface dermatitis with perivascular and peri appendageal inflammatory infiltrate, mucin deposition and basement membrane thickening DIF shows linear deposition of IgG, IgM and C3 at basement membrane zone
Traction alopecia	Early stages—there is perifollicular erythema, papules and pustules in the frontal and temporoparietal areas Scarring alopecia at sites of tight buns, ponytails, tight braids with fringe sign [13] Fringe sign—a strip of thin hair at the distal end of the patch (Fig. 14.6) [13]	Reduced hair density, absent hair follicles, hair casts, absent hair with brown outlined follicular openings	Increased catagen/telogen count Pigment casts Trichomalacia

(continued)

Table 14.1 (continued)

Disease	Clinical features	Trichoscopy	Histopathological findings
Trichotillomania	Bizarre or angular shaped patches of ill-defined hair loss with broken hair of varying length involving the frontoparietal region of the scalp, contralateral to the dominant hand (Fig. 14.7) Public hair, body hair or facial hair may be affected	Broken hair at different lengths, longitudinal split ends of hair, irregular coiled hair, follicular microhemorrhages and amorphous hair residue. I hair (modified black spots due to remnants of hair shafts arising from broken pulled hair) [14] Flame hair (proximal hair residue that remains after pulling anagen hair) Tulip hair (short hair with dark tulip-shaped ends) V sign (frayed hair) and yellow dots [15]	Numerous empty canals, trichomalacia, incomplete disrupted follicular anatomy clefts in the hair matrix, intraepithelial and perifollicular hemorrhages and intrafollicular pigment casts Hamburger within a bun sign [16]—vertically oriented split of hair shafts and proteinaceous material and erythrocytes are present in the split. Most of the follicles are in catagen with very few in telogen
Central centrifugal cicatricial alopecia/hot comb alopecia	Progressive focus of cicatricial alopecia starting on vertex and then spreading outwards Inflammation at periphery and centre—smooth, shiny and noninflamed with hair present in scarred areas Itching, pain and burning may be present	Peripilar gray/white halo that is a (specific and sensitive dermatoscopic sign) Honeycomb-pigmented network that represents the hyperpigmented rete ridges and the hypomelanotic dermal papillae Hair shaft variability white patches (follicular dropout and scarring) perifollicular erythema, concentric white perifollicular and interfollicular scales, black dots interfollicular-pigmented asterisk-like or stellate brown macules	Premature degeneration of IRS resulting in outward migration of hair shaft through the ORS at level of isthmus Lamellar fibroplasia, dense lymphocytic inflammation surrounding the follicle Follicular destruction and fibrous tract formation

Table 14.1 (continued)

Disease	Clinical features	Trichoscopy	Histopathological findings
Pseudopelade of Brocq	Irregularly defined and confluent patches of scarring alopecia	Lack of follicular ostia	Early stage—sparse or moderate lymphocytic infiltrate around the infundibulum and the absence of sebaceous glands are pathologic hallmarks Late the follicular epithelium becomes more and more atrophic and follicles are often surrounded by concentric lamellar fibroplasias until finally the follicle is replaced by fibrous tracts

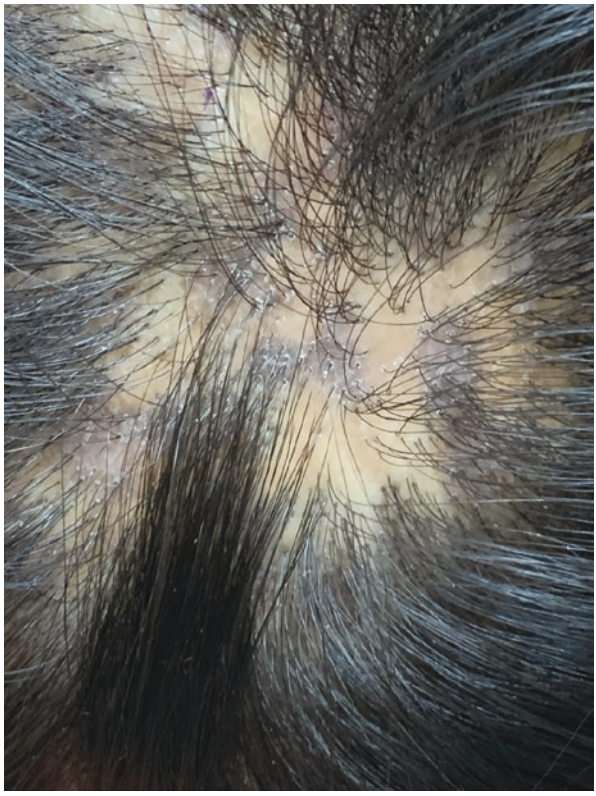

Fig. 14.4 Clinical picture of LPP with violaceous pigmentation, perifollicular scaling and scarring alopecia

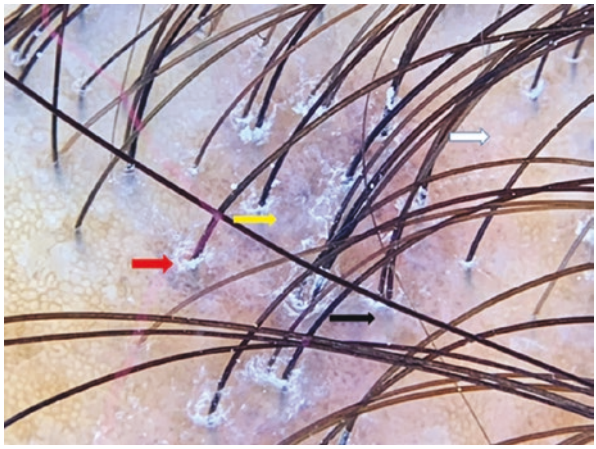

Fig. 14.5 Trichoscopic findings in LPP absence of follicular openings (white arrow); perifollicular scaling (red arrow); white structure less cicatricial areas (yellow arrow); perifollicular erythema (black arrow)

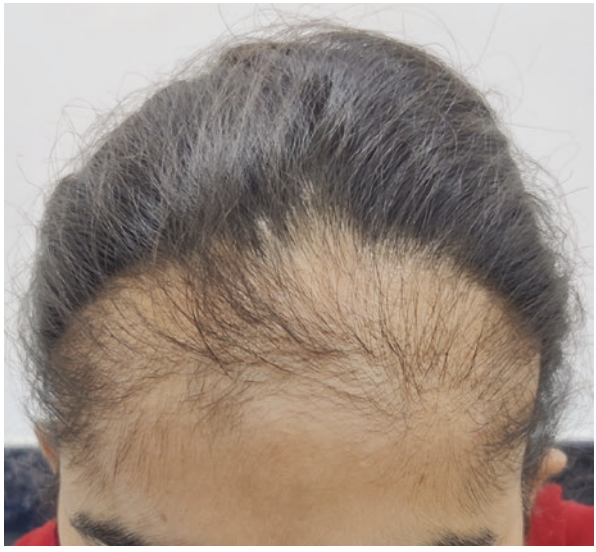

Fig. 14.6 Traction alopecia in a Sikh female with fringe sign

Rakowska et al. proposed major and minor dermoscopic criteria for the diagnosis of FPHL [17]. Major criteria include (1) more than 4 yellow dots in 4 images in the frontal area; (2) lower average hair thickness in the frontal area compared with the occiput; and (3) more than 10% of thin hairs (<0.03 mm) in the frontal area. Minor criteria include (1) increased frontal to the occipital ratio of single-hair pilosebaceous units; (2) vellus hairs; and (3) perifollicular discoloration. The diagnosis of FPHL is made when two major criteria or one major plus two minor criteria are present.

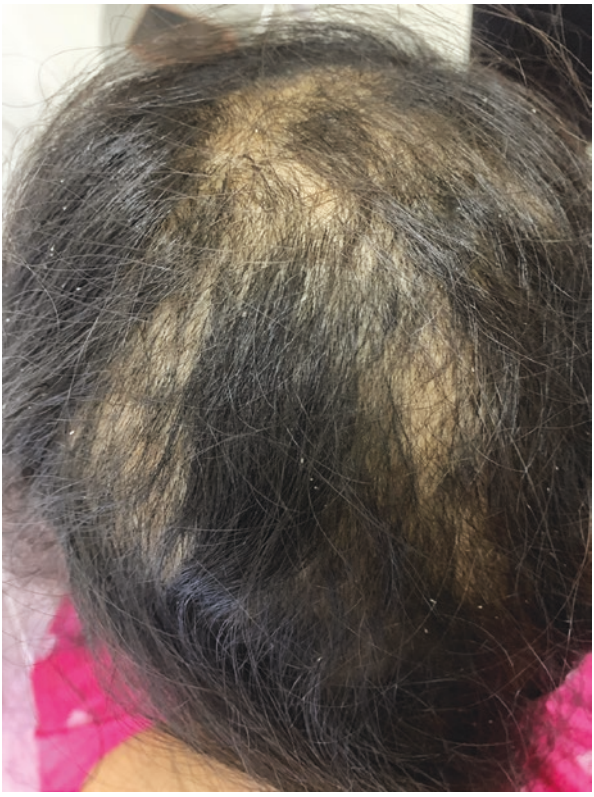

Fig. 14.7 Trichotillomania (scarring hair loss with hair broken off at irregular lengths with coincidental pediculosis capitis)

Hemogram, ferritin and thyroid function tests should be done in all patients with FPHL to rule out concomitant telogen effluvium due to iron deficiency disorder or a thyroid disorder. FPHL has been found to be associated with hyperandrogenism. Tests to rule out hyperandrogenism need to be done in patients with irregular menses, hoarse voice, hirsutism, loss of libido and clitoromegaly.

14.2.1.6 Treatment

Treatment of FPHL involves counselling the patient about its tendency for lifelong progression, with rates of progression being extremely variable, and ensuring compliance to treatment.

Topical minoxidil is the most commonly used drug for the management of FPHL. Minoxidil gets converted into minoxidil sulphate by the enzyme sulfotransferase present in the outer root sheath, leading to the opening of ATP-sensitive potassium channels which increase calcium entry into the hair follicle and inhibit

the epidermal growth factor (EGF)-induced inhibition of hair growth. Also, it increases the expression of hepatocyte growth factor (HGF) mRNA, increasing duration of the anagen growth phase. Minoxidil 2% lotion and 5% foam are FDA-approved treatments for FPHL. One mL of minoxidil is to be applied on the dry scalp twice a day. Patients should be counselled regarding the possibility of initial hair fall at 4–6 weeks due to early telogen release. Effect starts to appear at 4 months and the maximal response is noticed at 1 year. Side effects like irritation and hair growth on the face are the common side effects. Hypertrichosis is seen in 4% of the females and is reversible, reducing in 4–5 months. Contact dermatitis due to propylene glycol is also known to occur due to minoxidil. Minoxidil is contraindicated in pregnant and lactating females.

Other topical therapies include melatonin 0.1%, topical ketoconazole and topical prostaglandins analogue with varying results.

Women who respond poorly to monotherapy or who have signs of hyperandrogenism can also be given systemic medications. 5 Alpha-reductase inhibitors like finasteride and dutasteride have been tried in FPHL with varying efficacy. They are not FDA-approved for use in women and contraindicated in pregnant women and during lactation. Large scale studies on its efficacy for FPHL are limited. Finasteride can be given at dose of 2.5–5 mg with varying results.

Spironolactone is a synthetic steroid which acts by blocking androgen receptors and weakly inhibits androgen biosynthesis. It is given in doses of 50–300 mg/day. It is the most commonly used anti-androgen for the treatment of FPHL and hirsutism. Side effects include breast tenderness, menstrual irregularities and postmenopausal bleeding. The rise in BP and serum potassium can be seen in patients with renal failure.

Cyproterone acetate is an androgen receptor blocker. It also decreases the androgen synthesis and decreased uptake of androgen. It has been tried in doses of 50–100 mg/day for the first 10 days of each menstrual cycle. The side effects of cyproterone acetate are weight gain, breast tenderness, nausea and loss of libido.

Flutamide is a nonsteroidal anti-androgen which acts by inhibiting androgen uptake and inhibiting the nuclear binding of androgen within the target tissue.

Low-dose oral minoxidil is not often used in treatment of FPHL. In a randomized controlled trial, topical 0.75% adenosine containing lotion was found to increase the growth of anagen hair and thick hair in patients with FPHL [18].

Hair transplantation is usually not required but has been tried in FPHL and is successful in patients with limited hair loss and retain good hair density at donor sites. Camouflage and wigs are an easy alternative. Camouflage involves adding small fibers held in place electrostatically or dyeing the scalp the same color as the hair to create the illusion of thick hair. Wigs can be worn over the top of the existing hair and hairpieces can be interwoven with existing hair. Wig hair is made of acrylic fiber which withstands wear and tear or natural fiber which looks better, is easier to style and is long-lasting but more expensive.

14.2.2 Telogen Effluvium

Telogen effluvium is the second most common cause of hair loss in females. It is characterized by sudden onset diffuse shedding of approximately 100–1000 hair per day.

14.2.2.1 Etiopathogenesis

Telogen effluvium is caused by an abnormality in the normal hair cycle, which is triggered by numerous factors. Precipitating factors for telogen effluvium include stress, trauma, post Covid-19, anorexia nervosa, pregnancy, drugs, thyroid diseases, nutritional deficiency and acute febrile illness. There is a disbalance of TH1/TH2 cytokine balance during stress leading to change in hair parameters [19]. Also there is an inflammation of the small papillary or peripapillary vessels due to circulating immune complexes in patients with telogen effluvium secondary to SLE or post febrile illness [20]. It occurs 2–6 weeks after the onset of high fever, and usually lasts for at least 6 weeks. In about one-third of the cases, no triggering agent is found. The cause for the same is the sudden premature conversion of all anagen hair follicles into telogen hair leading to shedding of hair, after 3 months of the precipitating event. Headington [21] has described five functional types of telogen effluvium.

Immediate anagen release—Sudden damage of anagen hair due to chemotherapeutic drugs leading to shedding of hair.

Delayed anagen release—It is seen in telogen gravidarum. During pregnancy, there are high levels of estrogen which maintain the hair in anagen phase but at delivery, anagen hair turns into telogen, and after 2–4 months telogen hair is shed. It lasts for 2 months or may be longer. It is seen in 20% of women and not necessarily in all deliveries, but almost always after first delivery. This may be due to the stress-induced arrest of mitosis which is maximum during first delivery.

Short anagen syndrome—This is seen in androgenic alopecia where there is shortening in duration of anagen phase and telogen effluvium precedes visible balding of the scalp.

Immediate telogen release—This is seen after minoxidil therapy. Minoxidil stimulates exogen hair to release before development of anagen phase, hence after minoxidil therapy hair loss in noticed after 4–6 weeks.

Delayed telogen release—It occurs in animals with synchronous hair cycles during shedding of winter coats. It occurs due to prolonged telogen phase followed by transition to anagen phase.

However, there is a new classification given by Rebora et al. [22] to explain the pathogenesis of telogen effluvium.

14.2.2.1.1 Premature Teloptosis

It is similar to Headington's immediate telogen release. The effects seen during treatment with salicylic acid, retinoids and minoxidil can be explained by premature teloptosis. Retinoids cause the disruption of desmosomes and hemidesmosomes leading to detachment of keratinocyte and shedding. The shedding of hair after 4–6 weeks of minoxidil is due to the sudden release of telogen hair. It also supports the seasonal correlation of telogen effluvium with autumn. The UV radiation in previous summers caused cadherin disruption and shedding in autumn 2–3 months later.

14.2.2.1.2 Collective Teloptosis

It clubs Headington's delayed anagen and telogen release. It is used to describe the mechanism for hair loss seen in neonates, postpartum TE and hair loss due to non-cytostatic drugs. The occipital hair in neonates is in the telogen phase at delivery; hence, teloptosis (hair shedding) occurs 3 months after delivery, thus being responsible for transient neonatal hair loss. Estrogen, minoxidil and finasteride cause collective teloptosis on treatment cessation.

14.2.2.1.3 Premature Entry into Telogen Phase

This type may be equivalent to Headington's immediate anagen release. Here there is an anagen arrest usually due to an antimitotic insult. The hair loss depends on the duration, intensity of insult, the phase of the hair cycle during which insult took place and the preexisting hair disorder like Androgenetic alopecia. If the insult takes place during the anagen phase (I–V) the hair shed would be dystrophic. If the hair is in the near end of anagen phase (anagen VI), the hair will enter the telogen phase and will be shed as telogen hair after 3 months. If the insult is massive and lasts long enough, both the dystrophic and telogen type of hair loss will occur. It explains the hair loss due to chemotherapeutic drugs, nutritional insufficiencies and lymphocyte toxicity (autoimmune telogen effluvium). Autoimmune telogen effluvium is associated with thyroid diseases, Sjogren disease, inflammatory bowel disease and autoimmune atrophic gastritis.

14.2.2.2 Bedside Tests

The hair pull test in these patients is positive, with more than 10% of the hair being extracted from any part of the scalp. Hair trichogram shows more than 25% of the hair are in the telogen stage in acute phase.

14.2.2.3 Investigations

Investigations like hemogram, thyroid function tests, serum ferritin, vitamin B12 and vitamin D3 levels should be done to rule out the etiology of telogen effluvium. Histopathology of acute forms is nonspecific but in chronic telogen effluvium, only an increased telogen hair is detected.

Telogen effluvium may be acute or chronic when its duration exceeds 6 months.

14.2.2.3.1 Acute Telogen Effluvium

Acute TE is described as an acute-onset scalp hair loss occurring 2–3 months after a triggering event. The functional mechanism of shedding in majority of these cases is immediate anagen release. Majority of cases usually remit within a few months.

14.2.2.3.2 Chronic Telogen Effluvium (CTE)

CTE was described by David A. Whiting in 1996 [23]. It is idiopathic and seen in females aged 30–60 years. Patients present with sudden-onset diffuse shedding of hair enough to cause chunks of hair seen in the bathroom, brushes and combs. It is chronic with intermittent episodes of improvement. Hair pull test is positive. Hair wash test in which the total number of telogen hair and vellus hair shed is counted after shampooing has been found to be useful in differentiating CTE with FPHL. FPHL shows more than 10% of vellus hair (<3 cm) [23]. Various differentiating features between FPHL and CTE are given in Table 14.2.

Trichodynia has been found to be associated in 20% of patients. It occurs in sites where hairs are actually shedding and it may be regarded as a sign of severity of the disorder and of the possibility that TE may continue further, often more than 3 months.

Table 14.2 Differentiating features between FPHL and chronic TE [24, 25]

	FPHL	Chronic TE
Distribution	Central portion of scalp and preserved frontal hairline	Generalised
Onset	Gradual	Abrupt
Appearance	Hair thinning with wide midline part	Diffuse thinning
Hair shedding	Minimal	Prominent
Hair pull test	Usually negative (positive in active patients at frontal region	Positive at all sites
Other history	Family history +	H/O previous major illness or stress
Scalp biopsy	T:V ≤4	T:V ≥7
Hair wash test	Vellus hair >10%	Vellus hair <10%

14.2.2.4 Chronic Diffuse Telogen Hair Loss

It refers to telogen hair shedding, longer than 6 months, secondary to a variety of organic causes. Prominent causes include thyroid disorders, profound iron deficiency anemia, acrodermatitis enteropathica, malnutrition and drug induced.

The treatment for the acute telogen effluvium is the removal of the underlying cause. To find the cause it must be remembered that a lag of 3 months is present and patients may come when the cause of TE ceases to be active. Topical corticosteroids have been tried in patients with autoimmune telogen effluvium. There is no proven role of vitamins or supplements for any form of telogen effluvium. A treatment of CTE warrants ruling out other causes of CDTHL, including AGA, drug-induced hair loss, hypo- and hyperthyroidism, and chronic diseases. The treatment options for CTE are not many. Topical treatment which have effect on hair cycle can be tried.

14.2.3 Hirsutism

Hirsutism is defined as the growth of terminal hair in females in androgen-dependent areas. It is characterized by the growth of coarse pigmented long hair on the face, chest, abdomen, back and thighs. There are various causes for the same as mentioned in Table 14.2.

14.2.3.1 Severity Score

The severity of hirsutism is graded on the basis of modified Ferriman–Gallwey scoring (mFG) system. Each body site is scored on the basis of the severity of hair growth and all the scores are added to get the final score. mFG <8 is normal and >8 is considered hirsutism. mFG score 8–15 is considered mild hirsutism and score >15 is considered moderate to severe hirsutism.

14.2.3.2 **Investigations** (Table 14.3)

In women with locally excessive hair growth with mFG <8, androgen levels need not be measured [27]. However, in women with mFG >8; If sexual hair growth is moderate to severe or there is clinical evidence suggestive of hyperandrogenic disorder, early morning serum total and free testosterone should be tested. Menstrual irregularity, infertility, galactorrhea, central obesity, acanthosis nigricans, clitoromegaly and sudden onset or rapid progression of hirsutism are indicative of a hyperandrogenic disorder. Further investigations corresponding to the etiology should be done. If total testosterone is >200 ng/dL, the patient is evaluated for tumoral hirsutism, ovarian hyperthecosis and HAIR-AN syndrome.

Table 14.3 Causes of hirsutism with clinical features and investigations [26]

Cause	Clinical features	Investigations
Constitutional		
Familial	Facial with prolongation of preauricular implantation line	Normal
SAHA syndrome	Hirsutism (central or peripheral) Acne Intense seborrhea FPHL Oligomenorrhea or polymenorrhea	Mild increase in DHEAS or test testosterone normal
Endocrine organ based		
Adrenal hirsutism		
Congenital adrenal hyperplasia (21 α hydroxylase deficiency), cushing syndrome, adrenal tumors	Central hirsutism, virilization	↑ 17-OH progesterone ↑ DHEAS ↑↑ ACTH
Ovarian hirsutism		
PCOS, ovarian hyperthecosis syndrome, ovarian tumors	Lateral hirsutism, acne, seborrhea, obesity, menstrual disorders	↑ Free testosterone ↓ SHBG ↑ Estrone
Pituitary hirsutism		
Prolactin secreting pituitary adenoma, psychogenic drugs ectopic hormone production (small cell lung cancer; carcinoid tumor)	Amenorrhea, galactorrhea, FPHL, acne, seborrhea, both central and lateral hirsutism	↑ Prolactin, ↑↑ ACTH (in SCC lung and carcinoid tumor)
Drugs		
Anabolic steroids	Hirsutism on lateral aspects of the face and back	Elevated parent drug or metabolite in blood, urine or hair

14.2.3.3 Treatment

Treatment of hirsutism includes temporary modalities of hair epilating like waxing, sugaring, tweezers, plucking. Hair depilatory creams are thioglycolates which disrupt the disulphide bond in the hair, hence dissolving the hair. Side effects of the depilatory creams are sulphurous odor and irritant dermatitis.

Eflornithine cream irreversibly inhibits ornithine decarboxylase, which catalyzes the rate-limiting step for follicular polyamine synthesis. Effect starts to appear at 6–8 weeks. Permanent hair reduction is defined as attaining at least 30% reduction of terminal hair and sustaining this reduction for a period longer than complete growth cycle of hair follicles (4–12 months), depending on the body site.

Photo-epilation and electrolysis of hair follicle are the permanent methods of hair removal. Photo-epilation is preferred for women whose unwanted hair is auburn, black, brown and electrolysis for white or blonde hair. Various lasers like alexandrite, diode and ruby laser and Nd:YAG and IPL sources emitting

wavelengths between 500–1200 nm are available for permanent hair reduction. Precooling and paracooling is required during hair removal laser. Side effects of lasers are erythema, hyperpigmentation, burn and paradoxical hypertrichosis. Paradoxical hypertrichosis is mostly seen in patients with the Mediterranean or Middle Eastern background on the neck and face. Women with hyperandrogenism are at higher risk. Electrolysis involves electric current passing through fine wire electrodes, which is manually inserted sequentially into individual hair follicles. There are two techniques of electrolysis, the galvanic electrolysis technique and thermolysis technique which use direct current and alternating current respectively to target hair follicle. In women with hirsutism despite cosmetic hair removal methods, pharmacological therapy is desired. Women who are not seeking fertility should be started on oral contraceptive pills. OCP reduces hyperandrogenism by suppression of LH secretion, increasing SHBG by stimulating its hepatic production, and decreasing binding of androgen to its receptor. OCP with lower androgenicity progestins like desogestrel and gestodene and androgen receptor antagonists like drospirenone and cyproterone acetate are efficacious drugs. Antiandrogens like spironolactone dose of 50–300 mg/day, finasteride 2–2.5 mg/day and flutamide 25–300 mg/day are added to OCPs if there is no response to OCPs after 6 months of treatment. Due to their teratogenic potential, anti-androgens are not indicated in females with childbearing potential. However, in women who are not sexually active, have undergone permanent sterilization or are on long-acting reversible contraception, either OCPs or anti-androgen can be initiated as initial treatment.

14.2.4 Alopecia Areata

Alopecia areata is an autoimmune condition characterized by acute onset of well-defined patches of noncicatricial hair loss on the scalp, beard and eyebrows.

14.2.4.1 Epidemiology

With a lifetime prevalence of 2%, it is found in 0.1–0.2% of the population at a given time [28, 29]. All the ethnic groups and both the genders are equally affected. 70–80% of cases occur before the age of 40 years with around 48% of patients having the onset of disease in the first to the second decade [30].

14.2.4.2 Predisposing Factors

AA has a genetic predisposition for certain MHC classes like HLA DQB1*0301 and HLA DRB1*1104. A family history of AA is found to be present in 10–42% of patients. Genes encoding natural killer cell receptor D ligands and downstream effectors of JAK pathway influence AA susceptibility.

14.2.4.3 Pathogenesis

AA results from breakdown in immune privilege with assault on the follicle at the level of the bulb by CD8 lymphocytes. The peribulbar lymphocytic infiltrate induces hair follicle keratinocytes to undergo apoptosis that results in inhibition of cell division within the hair matrix and shaft formation.

14.2.4.4 Clinical Features

Patients present with well defined, smooth, round to irregular patches of hair loss (Figs. 14.8 and 14.9). Towards the periphery of the area of active hair loss, small 3–4 mm exclamation mark hair is seen. These are dystrophic hair with fractured tips due to inhibition of cell division of hair matrix at the level of hair bulb. If there is severe inhibition of cell division, there may be fracture of the hair shaft before emergence from the scalp, which are called black dots. White hair are often spared and hair are frequently white when they regrow.

Fig. 14.8 Patchy alopecia areata in a female

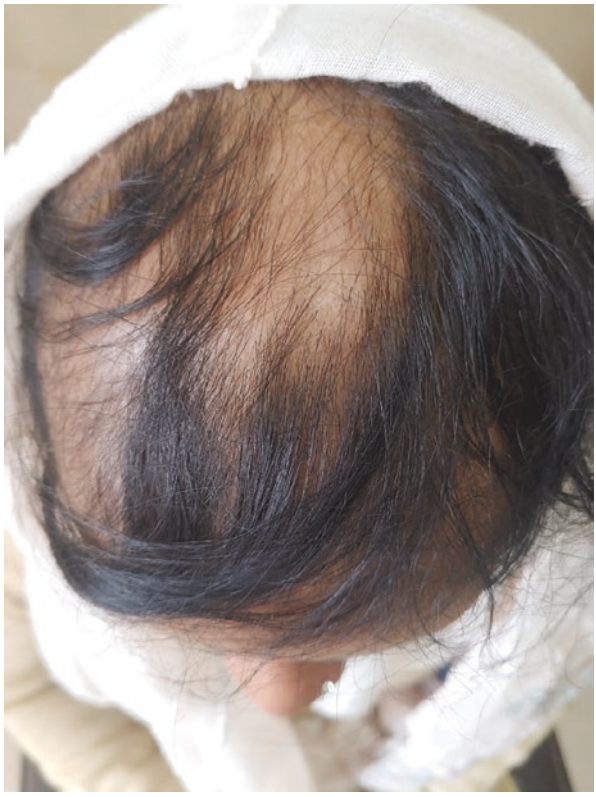

Fig. 14.9 Multiple patches of alopecia areata in a female

Marie Antoinette Syndrome/Thomas More Syndrome are conditions in which the scalp hair suddenly turns white. This condition is actually an acute episode of diffuse AA in which there is sudden whitening of hair due to preferential loss of pigmented hair. This condition has been named after Marie Antoinette, a French queen, whose hair allegedly turned white the night before her last walk to the guillotine during French revolution. Similarly Thomas More's hair turned white overnight in the Tower of London before his execution.

14.2.4.5 Variants of AA

There are different types of AA on the basis of severity, pattern and extent.

Based on extent

- Patchy (Figs. 14.8 and 14.9).
- Alopecia totalis (AT, whole scalp).
- Alopecia universalis (AU, all body hair affected).

Based on morphology

- Ophiasis—It is the pattern in which the hair loss occurs in the shape of a wave at the circumference of the head.
- Sisaipho—(ophiasis inversus) frontotemporoparietal region is affected with alopecia and occipital band being normal.
- Reticular—AA in a net-like pattern.
- Perinevoid (around nevi) and linear are two other unusual variants of AA.
- Acute diffuse and total alopecia—Sato Kwawamura et al. described this sudden-onset inflammatory non-cicatricial alopecia which has marked female predominance and is characterized by diffuse hair shedding without typical patches.

Based on prognosis (Ikeda's classification)

- Ikeda type I (no disease association)—It accounts for 80% of the cases, presents with single patches of alopecia in age between 20 and 40 years with single patch lasting less than 6 months and infrequent development to AT in less than 10% cases.
- Ikeda type II (associated with atopic disease)—accounts for 10% of the cases, presents with multiple patches of alopecia, reticular alopecia or ophiasis, present before 20 years of age with each patch last for more than 1 year and frequent development to AT in 75% cases.
- Ikeda type II-(prehypertensive type)—accounts for 5% of the cases. It presents with the reticular type of alopecia areata, usually in young adults from families with arterial hypertension. They develop into alopecia totalis in 40% of the cases.
- Ikeda type IV (associated with autoimmune endocrinopathy)—accounts for 5% of the cases. It affects people aged more than 40 years and has a chronic course.

Nail involvement has been found to be present in 2–44% of AA cases, with children more affected (40%) than adults (20%). Findings are geometrical nail pitting, sandpaper-like trachyonychia, punctate leukonychia, red lunula, thinning, Beau's line and onychomadesis. The nail changes may persist after the resolution of alopecia areata as 20 nail dystrophy. The nail changes may precede the onset of alopecia areata when it is termed as alopecia areata unguium.

14.2.4.6 Associations

Various conditions have been found associated with alopecia areata. Autoimmune diseases like autoimmune thyroid disease, vitiligo, pernicious anemia, celiac disease and lupus erythematosus have been found to be associated with alopecia areata. The risk of atopic dermatitis was high in children less than 10 years. AA is rarely associated with autoimmune polyendocrinopathy–candidiasis–ectodermal dystrophy (APECED) syndrome. It occurs due to mutation in the AIRE gene. It is characterized by the presence of two out of these disorders: Addison's disease, mucocutaneous candidiasis and hypoparathyroidism. Other features that can be

seen in APECED syndrome are chronic atrophic gastritis with pernicious anemia, hypogonadism, alopecia areata, autoimmune hepatitis and vitiligo. AA has also been found to be seen in patients on anti-TNF-alpha therapy. It has also been found to be associated with psychiatric disorders like major depression, generalized anxiety disorder, social phobia and paranoid disorder.

14.2.4.7 Investigations

Dermoscopy of alopecia areata is very characteristic (Fig. 14.10). Histopathology can also be done in doubtful cases.

14.2.4.8 Differential Diagnosis

The differential diagnosis of alopecia areata is patchy hair loss in syphilis and lupus erythematosus. Hence antinuclear antibody test and rapid plasma reagin test should be done in patients where other clinical findings support these diagnoses. Tinea capitis (black dot) and trichotillomania are other differential diagnoses of AA.

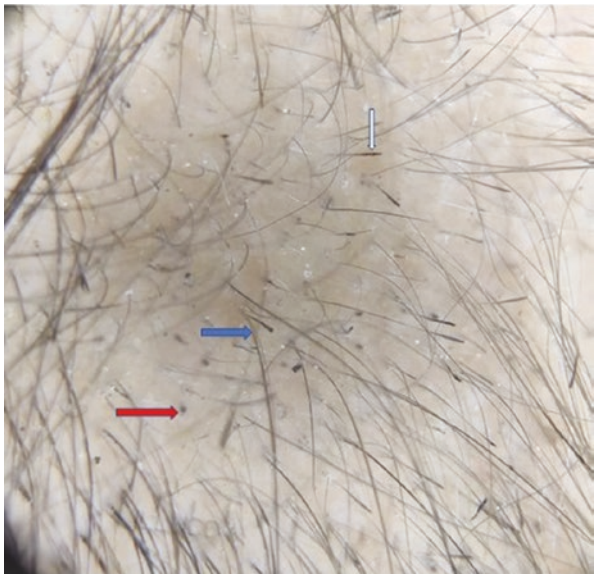

Fig. 14.10 Trichoscopic findings in alopecia areata—black dot (red arrow), tulip hair (blue arrow), exclamation hair (white arrow)

14.2.4.9 Treatment

Management of alopecia areata is based on the age group of the patient and surface area involved. Various topical agents like topical minoxidil, topical corticosteroids, calcineurin inhibitors and contact immunotherapy are used to manage alopecia areata.

Intralesional corticosteroid (ILC) in the concentration of 2.5 mg/mL (eyebrow and beard) and 5–10 mg/mL (scalp) given by jet injector or insulin syringe at 4–6 weeks interval is the best modality for patches in adults if the SALT score is less than 30%. The response to intralesional corticosteroids develops at 4–8 weeks. The intralesional steroids are given for a maximum of 6 months. If there is no response at 6 months, insufficiency of steroid receptors is considered. ILC are not to be used in children less than 6 years while in adolescents, ILC or topical corticosteroids can be used.

Topical corticosteroids can be prescribed as first-line topical treatment (alone or in combination) to treat scalp, eyebrow, or beard AA, mostly employed in young children.

In scalp AA, a potent topical corticosteroid should be applied daily for at least 6–12 weeks and, at most, 3–6 months.

Topical calcineurin inhibitors can be applied to treat scalp, eyebrow, or beard AA but should not be considered the first-line topical treatment, alone or in combination, for beard AA.

Topical prostaglandin analogues (e.g., bimatoprost or latanoprost) can be prescribed as first-line topical treatment (alone or in combination) to treat eyelash AA. It can be prescribed in conjunction with other topical or systemic agents, but it does not need to be used for all patients with AA.

Acute and widespread AA (>30%) are best treated with systemic corticosteroid therapy. Sharma proposed 300 mg oral prednisolone pulses at 4 weeks interval for 4 doses or till hair growth is observed [31]. Betamethasone oral pulse in the dose of 5 mg/kg on two consecutive days for a total duration of 12 weeks is found to be effective in alopecia areata [32]. Intravenous methylprednisolone at dose 500 mg once or 250 mg twice a day on three consecutive days every month has been found to be effective in extensive AA.

Topical immunotherapy with allergic contact sensitizers like diphenylcyclopropenone (DPCP) and squaric acid dibutyl ester (SABDE) has been effective in AA. These drugs modulate the T cell-mediated mechanisms responsible for AA and counteract the proinflammatory cytokines such as TNF-alpha, IL-10 and TGF-beta. SABDE is more effective than DPCP and has fewer side effects. However, DPCP is more stable in acetone and cheaper than SABDE. Dinitrochlorobenzene is mutagenic hence not commonly used. The extent of hair loss before therapy is the most

important predictor before effective treatment for DPCP. The remission rates with DPCP for multilocular AA were 43.8%, subtotal AA and ophiasis 33.3% and AT/AU 21.4%. Poor compliance, cumbersome to use, side effects, high cost and poor accessibility are major drawbacks of contact immunotherapy limiting its use.

Various immunosuppressive drugs like cyclosporine, methotrexate have been tried in reducing the activity of alopecia areata. Cyclosporine inhibits the activation of helper T cells pathogenic in AA and found to have regrowth at second to fourth week at a dose of 6 mg/kg/day for 12 weeks [33].

Newer drugs including JAK-STAT inhibitors like Tofacitinib and Ruxolitinib have been found to be effective in AA. In a study of 13 adolescents treated with tofacitinib, 9 patients had a significant hair growth of 93% at 6.5 months [34]. Intralesional PRP has also been tried in alopecia areata and found to increase hair growth [35]. The treatment algorithm for the management of alopecia areata is given in Fig. 14.10 [36].

14.2.4.10 Prognosis

Severe alopecia (AT/AU), presence of nail disease, young age at disease onset, presence of family history of alopecia areata, atopy, association with other autoimmune disease, ophiasis, and disease duration of more than 1 year suggest poor prognosis of disease. Spontaneous remission is seen in 30–50% patchy AA within the first 6–12 months of disease onset and 66% of patients show complete regrowth of hair within 5 years. The risk of relapse is 85% after 20 years. However, only 22.5% of AT will go into partial remission and 2.5% will go into complete remission. Five to ten percent of patchy AA progresses to AT/AU.

14.2.5 Lichen Planopilaris

Lichen planopilaris is among the most commonly diagnosed causes of scarring alopecia.

14.2.5.1 Epidemiology

It is seen commonly in the third–fourth decade of life. LPP is more common in females than males, with a ratio varying from 1:8 to 9:1.

14.2.5.2 Pathogenesis

It is an autoimmune disease in which T lymphocytes target the follicular antigen with the destruction of hair follicle stem cells. Recent studies suggested the role of PPAR —Gamma in the destruction of the pilosebaceous unit [37]. PPAR-gamma is decreased in LPP which leads to aberrant lipid metabolism in sebaceous gland leading to accumulation of toxic lipids which develop an inflammatory response and further scarring.

14.2.5.3 Clinical Features

Patients presents with patches of cicatricial alopecia (see Table 14.1). Cutaneous lesions of LP can be seen in 40% of the patients.

14.2.5.4 Investigations

See Table 14.1.

14.2.5.5 Treatment

Treatment options include findings based on case series or studies. *Ultrapotent Topical and intralesional steroids* are first-line therapy for active LPP. It is used twice daily for the first month, followed by a once-daily application for 3 months then every other day for 3 more months [38]. *Systemic steroids* at a dose of 1 mg/kg/day for 15 days tapered over 4 months is the second-line treatment in active cases but it has a high relapse rate of 80%. The can be used as monotherapy or in association with other topical and or systemic therapies. In extensive involvement, systemic steroids hydroxychloroquine, methotrexate and cyclosporine have been shown to be effective in Lichen planopilaris. Hydroxychloroquine 200 mg twice daily is the first-line systemic agent which may be switched to cyclosporine if manifestations continue after 3–4 months. In a RCT hydroxychloroquine 400 mg daily versus methotrexate at a dose of 15 mg weekly administered for 6 months in refractory LPP, there was a higher efficacy of Methotrexate over at 6 months than HCQ [39]. There was an improvement in perifollicular erythema, perifollicular scaling and follicular keratosis. The response rate to monotherapy to HCQ is 51% while methotrexate is 87.5%. In a retrospective study, mycophenolate mofetil at a dose of 0.5 mg twice weekly for 4 weeks and then 1 g twice daily for at least 20 weeks showed a complete response in 5 patients with 85% reduction in lichen planopilaris area index score [40]. Other agents tried in LPP are *pioglitazone*, *griseofulvin*, *oral tetracyclines*, *retinoids* and *thalidomide* with varying success.

There are two main clinical variants, viz. frontal fibrosing alopecia and Graham Little–Piccardi–Lasseur syndrome. *Frontal fibrosing alopecia* is seen in postmenopausal females. There can be eyebrow involvement in 73% and body hair has been found to be lost in 25% of patients. Topical steroids, calcineurin inhibitors, doxycycline, finasteride hydroxychloroquine, mycophenolate mofetil and UVB have also been used with disappointing results.

14.3 Hair Loss in Lupus Erythematosus

Lupus erythematosus (LE) is an important cause of hair loss in females. Hair loss is seen in about 50% of patients of SLE at some point in time. The hair loss in lupus can be specific (in which interface dermatitis is seen). This includes acute, subacute, discoid, tumid lupus erythematosus. Acute LE is characterized by patchy type of alopecia. Subacute LE manifests as polycyclic, annular or psoriasiform plaques with thick adherent scale resulting in patchy hair loss. Noninflammatory patches of alopecia are seen in tumid LE. Discoid LE in early stage is characterized by well-defined patches of alopecia with erythematous to violaceous surface follicular pugging, telangiectasia and scaling may be present. In late stages, dyspigmentation, follicular plugging and atrophic scarring is seen. DLE accounts for 30–40% of scarring alopecia [41]. DLE affects the scalp in 30–50% of patients and out of that 60% of the patients develop permanent and reversible hair loss. The age of onset is 20–40 years and is more prevalent in African American. Treatment of DLE includes photoprotection, broad-spectrum sunscreen, topical steroids lotion and topical calcineurin inhibitors. Systemic agents like hydroxychloroquine, chloroquine, acitretin, clofazimine and rituximab have also been tried. A patchy type of alopecia is seen in 14–50% of the patients of LE (Fig. 14.11) [42]. They can occur before, during or after the diagnosis of SLE. These patches have some degree of erythema and dermoscopic may show hypopigmentation and vessel changes. HPE shows atrophy of epidermis, hyperkeratosis, interface dermatitis and pigment incontinence. It responds to immunosuppressive therapy of LE.

Lupus nonspecific alopecia includes lupus hair and alopecia areata. Lupus hair are dry, fragile short hair on the frontal hairline seen in 5–30% of women with active phase of lupus and improves after LE flare subside. These occur as postulated due to hair shaft breakage and retarded hair growth. AA in SLE may show deep dermal mucin in histopathology and it has an unpredictable course. Telogen effluvium and anagen effluvium is also seen in lupus. Anagen effluvium occurs approximately 7 days. It may occur due to drugs like cyclophosphamide or methotrexate used in LE and flares of LE can cause rapidly dividing matrix cells to shut down during the active phase.

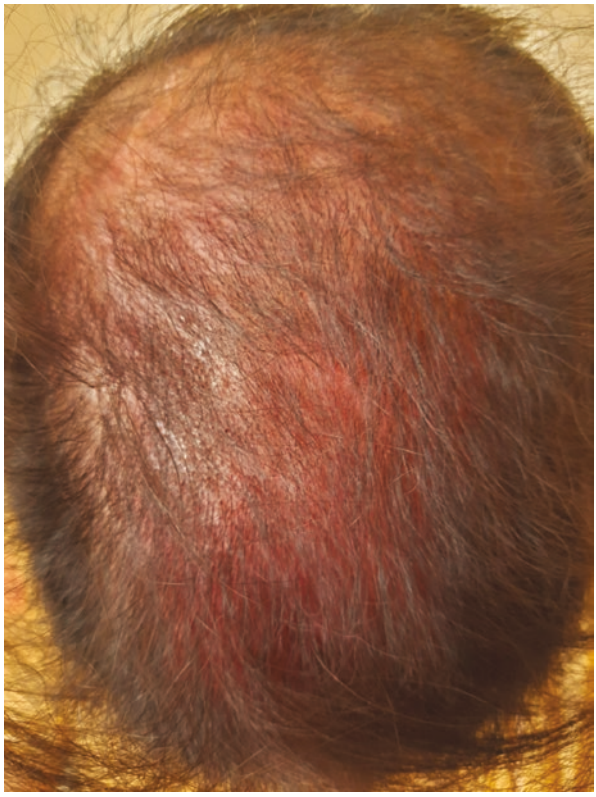

Fig. 14.11 Patchy alopecia in a patient of systemic lupus erythematosus

14.3.1 Pseudopelade of Brocq

Pseudopelade of Brocq is an idiopathic, chronic, slowly progressive patchy cicatricial alopecia.

14.3.1.1 Epidemiology

It is seen in women over 40 years of age.

14.3.1.2 Etiopathogenesis

The etiology and pathogenesis is not known.

14.3.1.3 Clinical Features and Investigations

See Table 14.1.

14.3.1.4 Diagnostic Criteria

Braun-Falco (1986) proposed the following clinical and histological criteria.

Clinical criteria
- Irregular and confluent patches of hair loss.
- Moderate atrophy (late stage).
- Mild redness around hair follicles (early stage).
- Female predominance (3:1).
- A long course of more than 2 years.
- Slow progression.
- Spontaneous termination possible.

Histological criteria
- No marked inflammation.
- No widespread scarring.
- No significant plugging of hair follicles.
- No sebaceous glands.
- Normal epidermis.
- Fibrotic streamers in dermis.

Immunohistochemistry
- Negative.

14.3.1.5 Prognosis

The course is the variable and alopecia is irreversible.

14.3.1.6 Treatment

No treatment stopped the progression. Autografting from nonscarred areas and surgical expansion can be done in severe cases.

14.3.2 Trichotillomania

Trichotillomania is characterized by a repetitive compulsive habit of pulling one's hair. Trichotillomania is listed in the Diagnostic and Statistical Manual of Mental Disorders—Fifth Edition (DSM-V) as an obsessive-compulsive and related disorders.

14.3.2.1 Diagnostic Criteria for Trichotillomania

1. The individual pulls their hair out on a recurrent basis, which results in hair loss.
2. Repeated attempts have been made to reduce or stop the hair pulling altogether.
3. The hair pulling causes significant distress or impairment in areas of occupational, social or other regions of functioning.
4. The hair pulling cannot be better attributed to another medical condition.
5. The hair pulling cannot be better explained as a symptom of another mental disorder.

14.3.2.2 Epidemiology

It is more commonly seen in adolescent females with the female:male ratio being 7:1. In childhood, young males are more commonly affected. It is a habit similar to thumb-sucking and nail-biting in children.

14.3.2.3 Clinical Features

The skin overlying the scalp is normal and hair is never completely lost within [1] the affected area, unlike alopecia areata (Table 14.1).

14.3.2.4 Investigations (Table 14.1)

Sometimes patients rarely present with Rapunzel syndrome. These patients present with nausea, abdominal pain, vomiting, obstruction with a hairball (trichobezoar) and intestinal perforation. Patients with insight should be referred to a psychiatrist or clinical psychologist.

Treatment of trichotillomania involves counselling, aimed at habit reversal along with pharmacotherapy using clomipramine or selective serotonin receptor inhibitors.

14.3.3 Traction Alopecia

14.3.3.1 Epidemiology and Pathogenesis

Traction alopecia is common in women of African origin due to curved hair follicle and cultural hairdressing practices prevalent there. The axial symmetry and helical shape give rise to geometric points of weakness making African hair more prone to breaking and tight hairstyles add the mechanical trauma to the hair shaft. Tight buns, ponytail hair extension and tight braids are highest risk hairstyles. Chemical relaxation of the hair through interruption of the disulphide bonds weakens the hair

shaft adds to a higher predisposition to TA. The mechanical damage induces inflammatory response which presents as perifollicular erythema with pustules and or papules in areas of friction. Chronic and repeated traction causes follicular damage and hair loss.

14.3.3.2 Clinical Features and Investigations

See Table 14.1.

14.3.3.3 Treatment

The main treatment is the relief of traction by loosening traumatic hairstyles, avoiding chemical and thermal treatment. Initial treatment includes the use of topical and intralesional corticosteroids and oral and topical antibiotics as anti-inflammatory agents. Minoxidil has also been tried in late stages. In advanced cases with scarring hair transplantation with techniques like punch grafting with rotation flaps, micro (1–2 follicular unit grafts) and mini (3–4 follicular unit grafts) grafting have been documented [43, 44].

14.3.4 Central Centrifugal Cicatricial Alopecia

14.3.4.1 Epidemiology

Central centrifugal cicatricial alopecia, also called hot comb alopecia, is seen commonly in women of African ethnicity. The female to male ratio is 3.

14.3.4.2 Pathogenesis

The condition has a multifactorial etiology involving both genetic and environmental causes. The traumatic hair practices in the African women predispose to this condition. It is called follicular degeneration syndrome due to premature degeneration of the inner root sheath.

14.3.4.3 Clinical Features and Investigations

See Table 14.1.

14.3.4.4 Treatment

Patients are advised to do minimal hair styling and grooming. Potent topical steroids may arrest progression and doxycycline or minocycline is useful in inflammatory cases with pustules. Minoxidil has been tried in these patients due to its similarity with FPHL.

14.4 Hair Shaft Disorders

Some hair shaft disorders present with increased hair breakage due to increased hair fragility. Monilethrix is a condition in which scalp hair is beaded along with follicular keratoses on the nape of neck and occiput. In Pili Torti hair is flattened and at irregular intervals completely rotated through 180° around their long axis. Netherton syndrome is an autosomal recessive disorder characterized by a triad of ichthyosis linearis circumflexa, atopy and trichorrhexis invaginata. Trichorrhexis invaginata involves the invagination of the distal part of the hair into the proximal portion appearing as bamboo hair. Trichorrhexis nodosa occurs in response to the hair shaft injury. It is an extreme form of withering. It occurs due to hairdressing procedures, shampooing, brushing. Congenital metabolic diseases like argininosuccinic aciduria, biotinidase deficiency and trichohepato-enteric syndrome can develop trichorrhexis nodosa. Trichothiodystrophy is characterized by hair shaft abnormalities due to decreased sulphur content along with lamellar ichthyosis, nail dystrophy and mental retardation and skin fragility. Polarizing light microscopy shows tiger tail appearance due to alternating dark and light bands.

Hair shaft disorders without increased fragility include pili annulati, uncombable hair syndrome, loose anagen hair syndrome, trichostasis spinulosa and Pili multigemini. Pili annulati is a normal incidental finding characterized by alternate dark and light bands due to split in the hair cortex. Woolly hair is tightly coiled hair associated with twists and grooves. They are common in Africans, found to be associated with congenital disorders like Naxos syndrome and Carvajal syndrome. Woolly hair nevus can present as can be localized patch of woolly hair along with congenital melanocytic nevus. Uncombable hair syndrome presents at 6 months to 12 years of age with silver coloured hair with a disorderly appearance. On light microscopy, the shaft has a three-dimensional aspect hence known as Pili trianguli et canaliculi. It is found to be associated with Neurofibromatosis and valproate therapy. Loose anagen syndrome is prevalent in children of 2–6 years of age, more commonly seen in females. It may present with decreased hair density, unruly hair or increased hair shedding. It occurs due to premature keratinization of the inner root sheath. Hair pull test is positive with Trichogram showing floppy sock appearance due to roughened cuticle, misshapen anagen bulbs and long tapered twisted

hair. It may resolve spontaneously. Minoxidil has been tried in many cases with variable results. Trichostasis spinulosa presents as vellus telogen hair on the face, trunk, limbs, interscapular area and found to be associated with the application of minoxidil and steroids, syringoma, epidermal inclusion cyst and chronic renal failure. Pili multigemini is when multiple hairs arise from multiple follicular structures but single pilosebaceous canal. It is associated with cleidocranial dysostosis.

14.5 Premature Canities

Premature canities means premature whitening of hair as a result of the ageing process. The age cutoff for premature canities is 25, 30 and 35 years in Caucasians, Asians and Africans, respectively [45]. There is early depletion of melanocyte reservoirs in the hair bulb; however, the nonmelanised melanocytes are still there in outer root sheath. Genetic syndrome-like Werner and Rothmund Thompson syndrome, nutritional disorders like kwashiorkor, autoimmune like pernicious anemia, atopy and thyroid disorders can lead to premature canities. The beard and moustache are the first to grey followed by scalp or body hair. On the scalp, temples are affected first followed by the crown and later to occur. Treatment includes camouflage, calcium pantothenate, PABA, PUVA-sol, melitane, topical prostaglandin analogues and antioxidants.

14.6 Pigmentary Disorders

Hereditary diseases like albinism, Waardenburg syndrome and piebaldism have whitening of hair. Vogt Koyanagi Harada syndrome and Allezendrani syndrome are the acquired causes of poliosis (localized patches of white hair). Drugs like chloroquine and hydroxychloroquine cause bleaching of the hair. Dithranol and chrysarobin stain light-coloured hair brown. Imatinib causes premature greying and skin hypopigmentation, and prostaglandin analogues cause darkening of eyelashes and iris. Nutritional deficiencies like copper deficiency in Menkes kinky hair syndrome cause achromotrichia. Intermittent protein transmission leads to the flag sign of kwashiorkor (*signe de la bandera*). Various metabolic disorders like phenylketonuria, homocystinuria and porphyria can cause altered hair pigmentation. The high concentration of copper in tap water or swimming pools can cause green color hairs. A yellowish staining of hair can be seen in heavy smokers and patients with exposure to picric acid dithranol.

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