and pilosebaceous testosterone available for conversion to DHT. This synergic action may explain why our patient did not show alopecia while taking triptorelin with tamoxifen. Moreover, minoxidil lengthened and enlarged the small vellus hairs and decreased shedding, highlighting the hypothesis of a relative hyperandrogenism as the cause of alopecia. Female sex hormone-binding globulin (SHBG) levels are inversely correlated with the grade of alopecia [5]. In our patient, the SHBG levels were low, potentially due to the AI effect.

Considering the pivotal importance of pharmacological castration in premenopausal endocrine-responsive BC patients and the widespread use of AIs in the metastatic and, probably in the near future, adjuvant settings, potential alopecia should not be a determinant in making clinical decisions. However, oncologists must be aware of such atypical adverse events for treatment planning, in order to highlight its consequent distress and to provide psychological counseling, especially in young patients.

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References


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Absence of chemotherapy-induced alopecia with paclitaxel in a case of hypothyroidism: case report

A 69-year-old woman presented in October 1998 with abdominal pain and distension. On physical examination, ascites and tenderness on palpating the lower abdominal area were found. An abdominal computed tomography (CT) scan revealed a 4.5 cm mass in the left ovary with multiple peritoneal implants and ascites. The serum tumor marker CA 125 was 190 U/ml (normal, <32), whereas thyroid hormones were within normal limits: thyroid-stimulating hormone (TSH) 5.1 U/ml, thyroxine 7.2 U/ml, triiodothyronine 1.2 U/ml.

She underwent a staging laparotomy and abdominal hysterectomy with bilateral salpingo-ophorectomy and omentectomy, stage IIIC disease was detected. Histology was consistent with serous cystadenocarcinoma grade 1–2. She received six cycles of chemotherapy with paclitaxel and carboplatin or cisplatin (alternate cycles). Toxicity was limited to grade 1 peripheral neuropathy with mild numbness in a glove-and-stocking distribution. No alopecia was evident at this point. At the end of chemotherapy, an abdominal CT scan showed complete radiological remission and serum CA 125 within normal limits.

One month later, she developed clinical signs of hypothyroidism, and TSH was 90 mU/l. On questioning, it appeared that the patient elected on her own to discontinue thyroxine replacement at the start of chemotherapy without informing the medical team. Thyroxine replacement therapy was recommenced and 2 months later thyroid hormones were within normal limits. As soon as thyroid function was restored, alopecia grade 2 appeared, 3 months after the completion of chemotherapy. Grade 2 alopecia was present for almost 2 months, after which hair regrowth was apparent.

Nine months later, the patient developed intra-abdominal relapse, and despite salvage treatment attempts, she died 3 months later from progressive disease.

The current case represents a very rare, probably unique, clinical entity. A possible explanation of the delayed onset of alopecia after the completion of paclitaxel chemotherapy could be attributed to the combined effects of thyroid hormones and chemotherapy upon the biological cycle of hair. Each hair follicle continually goes through three stages: anagen (growth), catagen (involution), and telogen (rest) [1]. Anagen is followed by catagen when hair follicles go through a highly controlled process of involution. Ultimately, the hair follicle enters the telogen stage when the hair shaft matures into a club hair which is eventually shed from the follicle [1]. The telogen stage lasts 2–3 months before the follicles re-enter the anagen stage and the cycle is repeated. At any given point, most of the hair follicles can be found in the anagen phase with only a small percentage in the telogen phase and just a few in the catagen phase (Figure 1).

Hair growth is influenced by many factors, including hormones, whose mechanism of action is not fully understood [2, 3]. Antineoplastic drugs disrupt the rapidly proliferating bulb matrix cells during the anagen stage. As a result, hair production ceases and the hair shaft becomes narrower with subsequent breakage and loss of hair; a phenomenon called anagen effluvium [4, 5]. Telogen effluvium is the excessive shedding of hair caused by an increased proportion of follicles entering the telogen stage. Low levels of thyroxine cause telogen effluvium [2].

In our clinical case, the patient was hypothyroid during chemotherapy with paclitaxel, due to the cessation of thyroxine replacement. As a result, most hair follicles probably entered the telogen stage (Figure 1). We hypothesize that paclitaxel could not act in the hair follicles that were in the telogen stage and thus no alopecia appeared (Figure 1). Once thyroid function was restored, it is likely that the telogen stage was completed leading to telogen...
effluvium, and alopecia grade 2 developed. Another factor that may contribute to the development of alopecia is the possibility of paclitaxel accumulating in the scalp and causing anagen effluvium. Since an increase in the percentage of follicles in the telogen stage leads to excessive shedding and telogen effluvium, drugs that reduce the percentage of hair follicles in this stage or prevent the evolution of hair follicles to this stage could be valuable in treating hair loss [3, 5].

In conclusion, the above clinical case represents a very rare clinical phenomena that shows an interesting interaction of two different factors in the regulation of hair growth. The mechanism of action and interaction of various factors such as thyroid hormones and chemotherapeutic agents in the biological cycle of hair growth is still poorly understood. Progress in our understanding of the biology and pathophysiology of hair follicles should lead to more effective therapies for disorders of hair growth, including chemotherapy-induced alopecia.

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References


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High incidence of severe hand–foot syndrome during capecitabine–docetaxel combination chemotherapy

5-Fluorouracil (5-FU) remains one of the most widely used chemotherapeutic agents in the treatment of malignancies of the gastrointestinal tract, breast, head and neck. The development of new 5-FU-related agents with improved anticancer effect is of significant clinical interest. Capecitabine (Xeloda®), a recently developed oral antineoplastic agent, has been demonstrated to possess enhanced antitumor effect and augmented tolerability over 5-FU [1]. This drug is being widely used on its own in the treatment of stomach, colorectal and breast cancers.

Grade 3 hand–foot syndrome, one of the major dose-limiting toxicities of capecitabine, has been reported in only 9.9% of patients with metastatic breast cancer undergoing capecitabine-only therapy who have previously undergone paclitaxel therapy [2]. Due to such a low percentage of patients experiencing this and other toxic effects, this drug is regarded as manageable and is not considered to have life-threatening toxicity. This agent is currently undergoing clinical trials on the feasibility of its application in combination with other agents. Taxanes have been shown to upregulate thymidine phosphorylase in vitro, and their toxicities have been shown not to overlap with those of capecitabine [3]. Combination chemotherapy utilizing capecitabine with a taxane has been proposed as a treatment for metastatic breast cancer and has been shown to be of great efficacy [4].

We administered capecitabine in conjunction with doxetaxel to patients with advanced gastric cancer for a total of four therapeutic cycles. Pyridoxine 300 mg was administered to these patients to prevent hand–foot syndrome. Nonetheless, grade 3 hand–foot syndrome was observed in ~52% (12 out of 23 cases) of the patients. This figure is far higher than the value of 24% reported for metastatic breast cancer patients [4]; ethnicity is suspected to