

Letters to the Editor

Evans's Syndrome: A Case Report and Review of the Literature

To the Editor: Evans's syndrome (ES) is a very rare disease, and was first described by Evans et al. in 1951.¹ The disease is characterized by concomitant or sequential occurrence of Coomb's positive autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (ITP). The first reported cases in Arabs were in Saudis.² Whereas the outcome of AIHA and ITP separately is good, the prognosis in the combination of these two conditions, i.e., Evans's syndrome, is poor. More cases of ES are described in adults than in children. We report a case of ES in a young Saudi boy, and provide a review of the literature.

Case Report

A 5½-year-old Saudi boy was admitted for the first time in September 1998 for the sudden onset of pallor and prostration. There was no history of ingestion of fava beans or any drugs. He did not have any illness suggestive of viral infections preceding this episode. He had never had a similar episode previously, neither were there any other cases of hemolytic anemia in any family members. On examination, the patient was pale and jaundiced. His anthropometry was appropriate for his age. His pulse was 166/min., respiration 58/min., temperature 38.9°C, and blood pressure 110/58 mm Hg. There was no skin rash. Cardiovascular, respiratory and central system examinations were within normal limits. There was no lymphadenopathy or hepatosplenomegaly.

Investigation showed hemoglobin of 5.5 g/dL, red blood cells of $1.71 \times 10^{12}/L$, mean corpuscular volume (MCV) 82 fl, mean corpuscular hemoglobin (MCH) 29.1 pg, mean corpuscular hemoglobin concentration (MCHC) 35.5%, white blood cells $5.8 \times 10^9/L$ with normal differential counts, and platelets $298 \times 10^9/L$. Reticulocyte count was 1.2% initially, rising to 20% later on. His blood group was A rhesus positive and direct Coomb's test (DCT) was strongly positive. There was no hemoglobinuria. Urea, creatinine and electrolytes were normal. Serum indirect bilirubin was 126 $\mu\text{mol}/L$, but other liver function parameters were normal. All hepatitis markers were negative. Mycoplasma titer was negative. Antinuclear factor (ANF) was also negative. His G6PD (glucose 6 phosphate dehydrogenase) level was $148 \text{ mU}/10^9$ red blood cells, which was normal.

Urgent blood transfusion was advised, but a similar and compatible blood group to the patient's was not available. The patient's hemoglobin level dropped further to 3.1 g/dL the next day. He was transfused with the least incompatible group O rhesus negative blood under cover of intravenous

methyl prednisolone. Corticosteroid was continued for two weeks after blood transfusion. The child was diagnosed with autoimmune hemolytic anemia of unknown etiology. He was discharged after two weeks with hemoglobin of 10 g/dL and no more hemolysis, and with the recommendation of regular follow-up in our outpatient clinic.

He failed to attend the outpatient clinic but was admitted one-and-a-half years later in February 2000 at the age of seven years, with a history of epistaxis and multiple bruises. Clinical examination showed no pallor or jaundice, but multiple bruises and petechial rashes all over the lower limbs. There was no lymphadenopathy or hepatosplenomegaly, and all systems were normal. Complete blood count showed hemoglobin of 10.7 g/dL, hematocrit 0%, red blood cells $3.6 \times 10^{12}/L$, WBC $5.15 \times 10^9/L$, reticulocytes 12% and platelets of $4 \times 10^9/L$. Prothrombin time and activated partial thromboplastin time were normal. DCT was strongly positive. Bone marrow examination showed increased erythropoiesis with increased number of normoblasts. There were some elements of megaloblastic changes. Myeloid:erythroid ratio was 2.4:1 (normal 5:1). Megakaryocytes were increased in numbers and were hyperactive. Cytoplasm was adequate with platelet formation. There was no extramedullary cell. A diagnosis of autoimmune hemolytic anemia with immune thrombocytopenic purpura (Evans's syndrome) was made. He was treated with intravenous immunoglobulin 400 mg/kg/day for five days, along with prednisolone 2 mg/kg/day for two weeks. His platelet count rose to $195 \times 10^9/L$. He was discharged home with a tapering dose of prednisolone for another two weeks and followed up in the outpatient clinic. Since then, he has had no more attacks of hemolytic anemia or thrombocytopenic purpura, but he is under regular follow-up.

Discussion

Evans's syndrome is a rare disease in which autoimmune hemolytic anemia and immune thrombocytopenic purpura, without a known underlying etiology, coexist. Experiences in pathophysiology, clinical presentation and management are available, with more cases in adults than in children. Many of the cases and the related literature have been reported from Japan. Some cases of ES have been reported in association with recurrent venous thrombosis³ and Graves' disease⁴ in adult patients. Abnormal thyroid functions with antithyroid antibodies were also found in 40% of cases of ES in one study.⁵ They studied the thyroid function tests separately in ES, AIHA and ITP, and confirmed the high prevalence of abnormal thyroid function tests in patients affected by AIHA, ITP and ES. The study also demonstrated the higher prevalence of autoimmune hypothyroidism in ES, and led to the possibility of including ES as one of the multiple autoimmune syndromes. Marked decrease of CD4+CD45RA+ cells was reported in one case of ES from

Japan, which was increased to normal level along with the remission of the disease with treatment,⁶ suggesting that these cells may play an important role in the pathogenesis of ES. Autoimmune neutropenia has also been reported in association with ES.⁷ It has also been reported to be induced by diclofenac.

Although steroids and immunoglobulins remain the mainstay of treatment of this condition, failure of response is not uncommon and prognosis remains unfavorable. Various methods of treatment have been described in the literature for those who are not responding to steroids. Cyclosporine A was successfully used in a case of ES, which was refractory to therapy including prednisolone, danazol, azathioprine, cyclophosphamide, vincristine, gammaglobulin and splenectomy. Danazol was also used with good response in a 66-year-old man with ES who was refractory to prednisolone. Another Japanese study stated that their herbal medicine *Sairei-to* granules (several water-soluble plant extracts) worked well in a case of steroid-resistant ES.⁹ They claimed that it has no side effects. A five-year-old boy with ES was reported to go into remission with marrow ablation followed by rescue with an HLA-identical sibling cord blood transplant.¹⁰ Another study suggested that medical treatment with combination agents¹¹ (intravenous immunoglobulin, steroids, vinca alkaloids, androgens and possibly cyclosporine) might provide a useful therapeutic approach to patients with ES.

So far, there is no consistent mode of treatment for those who fail to respond to steroids and immunoglobulins. Our patient has responded to these and so far has remained without any further episode of hemolysis or purpura, but he needs regular follow-up for a longer period of time.

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A Case of Recurrent Peripartum Thyroiditis

To the Editor: Postpartum thyroiditis (PPT) is a benign, often self-limiting disease. The classical form is a transient hyperthyroidism at 14 weeks' postpartum, followed by a transient hypothyroidism at 19 weeks.^{1,2} It has a 70% chance of recurrence during the subsequent postpartum periods.³ As there is only sparse data on the recurrence of PPT,² we thought of presenting this unusual case of recurrence during pregnancy itself.

Case Report

A 35-year-old Omani female presented to our clinic at 14 weeks' postpartum, with symptoms of palpitations, excessive sweating, generalized tremors, body aches and weight loss. There were no associated symptoms such as fever, vomiting, etc. She was multiparous, with eight children. Her past medical history was unremarkable. No similar problem had been seen during the previous postpartum periods, and she had not reported any problem during her last and previous pregnancies.

Physical examination revealed a young woman of average build, who looked distressed and anxious. Her temperature was 37°C, pulse 140/min, and BP was 150/100. She was not pale and the skin was normal. Her thyroid gland was enlarged but not tender. There was no exophthalmus, lid lag or lid retraction. There were fine tremors at both extended hands and tongue. Cardiac examination revealed a regular rhythm with sinus tachycardia and no murmurs. The chest, abdomen and neurological examination revealed no abnormality.

Investigations showed Hb of 11 g/dL, WBC 3.2/mm³, lymphocytes 51.9%, and ESR of 30 mm/h. There was laboratory evidence of thyrotoxicosis. Serum-free thyroxin concentration was >77.2 pmol/L (reference range 9.2-23.9). Serum thyroid-stimulating hormone (TSH) was <0.03 mIU/L (0.03-5.0). Thyroid scan and radioactive iodine uptake was a low 0.035% (reference range, 1-4%). Thyroid antibodies were positive for antithyroglobulin antibody (ATA) at 1:80 (reference range, 1:40) and antimitochondrial antibody (AMA) was at 1:6400 (reference range, 1:80). These findings were consistent with the diagnosis of PPT. The patient's symptoms were controlled with beta blockers for a period of two months.

Six weeks later, the patient was asymptomatic. Her pulse dropped to 80/min, but her blood pressure was still high at 170/100, and her thyroid gland was still enlarged. The thyroid function tests changed to a hypothyroid picture. Her free T₄ dropped to 3.0 pmol/L (9.2-23.9) and TSH increased to 26.7 mIU/L (0.32-5.0). Ten months later, both free T₄ and TSH returned to normal without any medication.

Sixteen months later, the patient presented again to the clinic at 12 weeks of a subsequent pregnancy, because of recurrence of her previous symptoms. On examination, she presented with similar findings of a rapid pulse of 140/min., BP at 150/100, an enlarged non-tender thyroid gland, and no exophthalmos, lid lag, or lid retraction. There were fine tremors over the extended arms. Apart from a gravid uterus of about 13 weeks' gestation, all other systems were normal.

Investigations of her thyroid functions revealed elevated free T₄, 27.7 pmol/L (9.2-23.9) and low TSH of <0.03 mIU/L (0.32-5.0). Antithyroglobulin antibodies (ATA) were negative, but antimitochondrial antibodies (AMA) were positive at 1:400. Thyroid scan was not done because of the pregnancy. One month later (at 16 weeks' gestation), she again became asymptomatic. Her thyroid function tests revealed a drop of free T₄ to 5.3 pmol/L and elevation of TSH to 10.50 mIU/L, which subsequently reverted to normal.

Discussion

Our patient showed the classical presentation of postpartum thyroid dysfunction (PPTD). She had a transient hyperthyroidism at 14 weeks' postpartum, followed by transient hypothyroidism at 19 weeks.^{1,2} During the subsequent pregnancy, the same biphasic features of the disease recurred during the early second trimester with a positive AMA. Her BP was also high.⁴

There are many causes of thyroid dysfunction that can occur during the first trimester of pregnancy, with a slight increase in free T₄ level and decrease in TSH concentration.⁵ Transient subclinical hyperthyroidism occurs in 10%-20% of normal pregnant women during the period of highest serum HCG concentrations.⁶ Our patient had a biphasic clinical picture during the second trimester of pregnancy, which passed on to a hypothyroid state after one month. She was unlikely to be suffering from Graves' disease, due to the absence of other features of this disease, such as ophthalmopathy and pretibial myxedema,⁵ besides the short duration of her symptoms. However, diseases such as Graves' disease and hashitoxicosis cannot be excluded without a thyroid scan, which is not possible during pregnancy. This patient was unlikely to be suffering from the syndrome of transient hyperthyroidism of hyperemesis gravidarum, which should be considered in a

woman with the same symptoms plus excessive vomiting and biochemical evidence of hyperthyroidism.⁷ In the latter, there is no history of thyroid illness preceding pregnancy; goiter is usually absent and thyroid antibodies are negative. The condition usually resolves spontaneously by 18 to 20 weeks' gestation.⁵ The patient was also unlikely to be suffering from hyperthyroidism, which can occur in women with gestational trophoblastic disease, such as hydatidiform mole and choriocarcinoma, which are generally associated with HCG levels more than 1000 times the normal.⁵ Her pregnancy progressed normally, and the ultrasonography showed no evidence of these two conditions. As well, the patient did not show features of subacute thyroiditis. Her thyroid gland was not tender, there were no systemic symptoms of inflammatory disease and no history of antecedent upper respiratory infection.⁸ In addition, she had positive thyroid immunoglobulins. A low uptake thyroid scan is diagnostic, but a thyroid scan is contraindicated during pregnancy. Thus, the diagnosis must be based on the clinical presentation and absence of thyroid-stimulating immunoglobulins.

Other causes of thyrotoxicosis include toxic multinodular goiter (which is uncommon during the child-bearing years), and rare conditions such as TSH-dependent thyrotoxicosis and exogenous thyrotoxicosis. Little information is available regarding the influence of pregnancy on the course and prevalence of these disorders.⁹ Struma ovarii and ovarian teratoma containing thyroid tissue are also extremely rare causes of thyrotoxicosis during pregnancy.⁵

Although a lot of studies indicated recurrence of PPT during the postpartum period,^{3,10-13} none of these studies indicated recurrence during pregnancy itself. Probably a more general term, such as peripartum thyroiditis, is needed to explain this unusual form.

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Mediastinal Widening Due to Lipomatosis and Herniated Liver and Stomach

To the Editor: We read with interest the article of Dr. Al-Adsani et al.¹ We experienced a similar case of a mediastinal lipomatosis of a 34-year-old man whose chest x-ray showed a huge pseudocardiomegaly (Figure 1).² CT scan revealed a large mass (Figure 2) of fatty attenuation (100-120 Hounsfield units) involving the mediastinal space from the T₃ level to the hemidiaphragm. This mass was hypodense and septated. There was no displacement of the mediastinal structures. Our patient had not received steroids and was not obese. We do not know the real cause of this diffuse mediastinal lipomatosis. However, the patient was operated on because of dyspnea on exertion, and the surgeon removed 5 kg of fat. Pathologic examination revealed mature fat tissue without nuclear atypia.

Mediastinal lipomatosis is a benign condition characterized by a large amount of mature adipose tissue within the mediastinum.³ It widens the mediastinum and may simulate mass lesions, thus leading to diagnostic errors. We found 36 cases of mediastinal lipomatosis reported in the literature. All the reported cases had in common some evidence of clinical Cushing's syndrome (either primary or iatrogenic), but not in our case.

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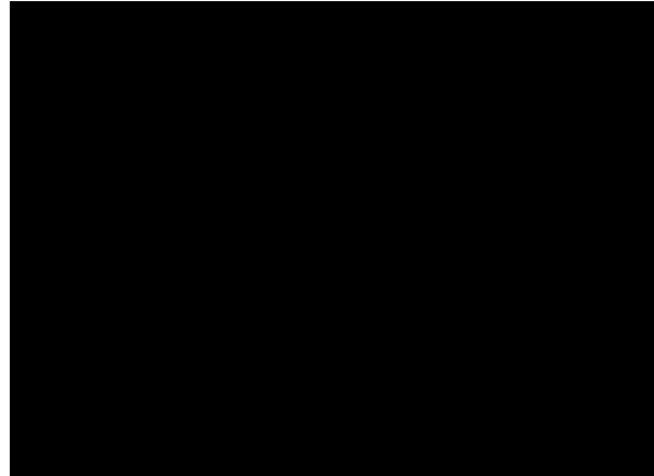


FIGURE 1. Chest x-ray shows a huge pseudocardiomegaly.

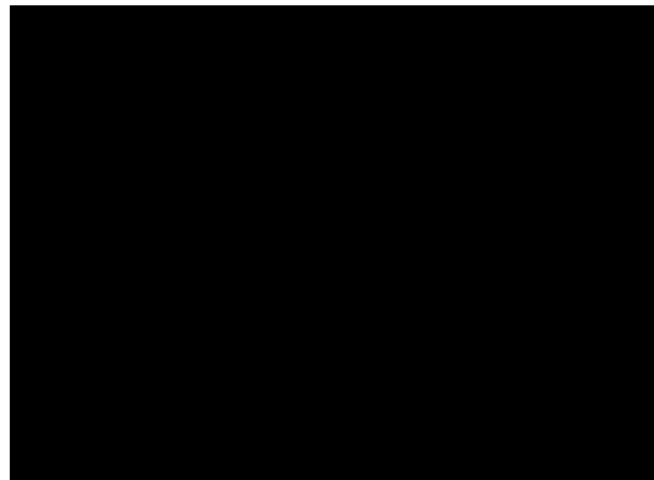


FIGURE 2. CT scan revealed a large mass of fatty attenuation.

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Reply

To the Editor: We would like to thank Dr. Hoeffel and associates for their letter regarding our article. We agree with them that mediastinal lipomatosis is a benign condition which widens the mediastinum and stimulates mass lesions, thus creating a challenging clinical problem. In most cases, definitive diagnosis can be established by CT. Although it is most commonly associated with Cushing's syndrome, steroid therapy and obesity, we agree

that it may present in patients without obesity. We believe that this uncommon presentation necessitates further study to identify the etiopathogenesis of this challenging condition.

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Strangulations Caused By Electric Car Sun-Roof and Windows

To the Editor: There is an increasing number of cases of accidents involving children in stationary vehicles in Saudi Arabia, but unfortunately, there appears to be a paucity of published studies. The previously hand-operated functions of motor vehicles are now being replaced by electrically powered gadgets for the convenience of the driver and the passenger alike. These convenient introductions have brought in their wake potential hazards to children. We have encountered two children in whom strangulations from electric car window and sun-roof, respectively, proved fatal in one and nearly so in the other. Our report focuses attention on the inherent dangers of such preventable accidents involving unsupervised children in motor vehicles.

Case 1

An eight-year-old boy was admitted with a history of his neck accidentally getting caught in the sun-roof of the family saloon car. He was standing on the driver's seat and playing with the control panel with his foot when he inadvertently activated the sun-roof mechanism which trapped his neck. He sustained injuries to his neck and vomited twice. On examination, he was semi-conscious and ill-looking with a temperature of 39.5°C, but he responded to painful stimuli. The face was cyanosed, with redness of the eyes, and compression red marks on the anterior aspect of the neck and a Glasgow coma scale of 9. He was hypotonic and the reflexes were depressed. Fundoscopy was essentially normal. His respiratory rate was 60/min., with bilateral medium coarse crepitations greater in the right than in the left lung. He had BP of 100/70 mm Hg, a pulse rate of 92/min. and normal heart sounds. Other systems were essentially normal. Arterial blood gases were pH 7.531, PaCO₂-55 mm Hg, PaO₂ 72 mm Hg, HCO₃ 26.6 mm Hg and oxygen saturation of 95%. Chest x-ray revealed bilateral diffuse patchy consolidations mostly on the right upper, middle and bilateral lower zones. Brain CT scan was normal. The patient required intensive care unit management for five days. He made a complete recovery with no residual neurological deficit, and was discharged 11 days later.

Case 2

A five-year-old boy was rushed to the emergency room in a comatose state. He was found with his neck caught in the power-operated window of the family 4-wheel drive vehicle for an unspecified period of time. He was said to have been playing with the automatic window of the vehicle. On arrival at the hospital, he was pulseless with unrecordable BP and was immediately intubated and resuscitated. The pulses feebly returned and he began to breathe shallowly 10 minutes later. On clinical examination, the face was swollen and cyanosed, with redness of the sclerae. There were red marks over the anterior, lateral and posterior aspects of his neck. The pupils were dilated and barely reacted to light. He remained unconscious and barely responded to painful stimuli, with a Glasgow coma scale score of 3. Fundal examination was normal, but the reflexes could not be elicited. Chest examination revealed medium scattered coarse crepitations. His BP at this stage was 100/80 mm Hg and other systems were essentially normal. He was transferred to the intensive care unit for further management. The arterial blood gases were pH 6.77, PaCO₂ 66.5 mm Hg, HCO₃ 11.7 mm Hg, and an oxygen saturation of 78.8%. Brain CT scan could not be done immediately, but was later normal. He progressively became spastic, could not be weaned off the ventilator and tracheostomy was carried out. He remained stable requiring tube feeding and full nursing care. He survived for 14 months and succumbed to pneumonia and massive bleeding from the tracheostomy.

Discussion

An aspect of motor vehicle-related accidents which has not become apparent or made an impression on the community is that involving children left unsupervised in stationary motor vehicles. These vehicles are often left with either the keys in the ignition, or the children somehow manage to access the keys and use them to activate the electrical system. In the two reported cases, the children were unsupervised in the vehicles and operated the sun-roof and the windows which resulted in their injuries. Reports of strangulation due to "one touch" electrically and mechanically operated car windows have been reported,^{1,2} with accompanying mortality,³ but that of the sun-roof has not to our knowledge been previously reported. The awareness of the dangers and fatalities from electrically operated garage door openers has resulted in the introduction of the reverse mechanism which allows re-opening of the door when it strikes any object.⁴

Unfortunately, there do not currently appear to be any reverse devices in motor vehicles sold in Saudi Arabia. The motor vehicle manufacturers probably have not deemed it essential to introduce the reverse mechanisms as it could be argued that these one-way operated devices themselves

enhance security against unlawful entry to the motor vehicles. We would therefore like to make the following recommendations. First, parents and guardians should be alerted to the potential hazards of these electrically operated devices in vehicles and the inherent dangers of leaving children unsupervised in these vehicles.⁵ Second, parents should be reminded of the importance of not leaving keys in the ignition with the children unattended in motor vehicles. Third, there is also the need for health professionals to bring such vehicle injuries to the attention of the public and the motor vehicle industry alike. Finally, it is suggested that the motor manufacturers should introduce into Saudi Arabia motor vehicles with reverse mechanism on windows and sun-roofs. The prevention of these types of catastrophes lies essentially with more public education and awareness.

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Second Cancer Risk in Hairy Cell Leukemia

To the Editor: Hairy cell leukemia (HCL) is a chronic malignant lymphoproliferative disorder accounting for about 2% of all leukemias.¹ A wide variety of second tumors have been reported in patients with HCL, with an incidence of about 8.7%.² We report two cases of HCL that were treated with alpha interferon (IFN- α) and INF 2-chlorodeoxyadenosine (2-CDA) and subsequently developed secondary cancer. These two cases signify that HCL patients appear to be prone to second malignancies. Close monitoring of cancer in HCL patients is advisable.

Case 1

A 66-year-old male with a history of three packets a day smoking for a year and social drinking (1-2 beers/month) presented with pancytopenia in the mid-1990s. Physical examination revealed a significantly enlarged spleen. Peripheral counts included hemoglobin of 8.7 g/dL, platelet count of 117,000/mm³, and leukocyte count of 2100/mm³, with 9% segmented neutrophils, 87% lymphocytes and 4%

monocytes. Peripheral blood smear revealed lymphocytes with morphologic features of hairy cell (HC). Bone marrow aspiration and biopsy were 55% cellular, with an atypical lymphoid interspersed throughout the sections. A diagnosis of HCL was made. Due to significant pancytopenia, splenectomy was performed which resulted in hematological remission. The spleen showed a diffuse lymphoid infiltrate involving the red pulp and some infiltration in the white pulp.

The patient remained in remission until 1991, when he relapsed with thrombocytopenia and neutropenia. He was treated with IFN- α (3 x 10⁶ U/3 times/week x 12 weeks subcutaneously), followed by 2-CDA (4 mg/m² intravenously x 12). In October 1995, he developed a tooth abscess. Further workup led to a diagnosis of squamous cell carcinoma of the left submandibular gland (T3N2b). Radical neck dissection was done and 3 of 47 lymph nodes were positive. He received radiation therapy (5760 cGy), which he tolerated well.

In August 1996, he presented with multiple (0.5-1 cm diameter) subcutaneous nodules on the inferior aspect of the chin. His CD4 cell count was 94/mm³ at that time. Biopsy of a nodule revealed poorly differentiated squamous cell carcinoma. He underwent surgical resection of the nodules followed by skin grafting and was also offered radiation therapy. He expired in March 1997 due to infectious complications.

Case 2

During a preoperative evaluation for left inguinal hernia in November 1989, a 60-year-old man was found to have a leukocyte count of 2800/mm³, hemoglobin level of 14.8 g/dL and platelet count of 159,000/mm³, with a differential of 48% segmented neutrophils, 43% lymphocytes, 2% monocytes, 2% basophils, and 1% eosinophils. There was no previous history of smoking or alcohol abuse. The following year, he presented with a worsening leukopenia and thrombocytopenia and splenomegaly. A diagnostic splenectomy was done. On the basis of the morphology of the spleen and the finding of TRAP (tartrate-resistant acid phosphatase) positive HC, a diagnosis of HCL was made.

Treatment with IFN-alpha was instituted (3x10⁶ U/3 times/week/subcutaneously x 12 weeks). His platelet count improved subsequently. Bone aspiration and biopsy performed in August 1991 showed HC infiltration in at least 75% of the marrow, where it replaced hemopoietic precursors and formed the typical "cobblestone" pattern. The patient was started on 2-CDA (4 mg/m² intravenously x 12 cycles). Following 2-CDA therapy, bone marrow aspiration and biopsy revealed a complete remission of the marrow.

In September 1994, the patient developed pain in the right side of his neck associated with difficulty in turning his face. CT scan of the neck showed asymmetry at the base of the tongue, with a swelling on the right and a solitary nodule in the left lobe of the thyroid gland. A biopsy of the

right neck mass and lymph nodes revealed a poorly differentiated squamous cell carcinoma. Chemotherapy including cisplatin (80 mg/m²) and 5FU (1000 mg/m²) was administered. After cycle one, the patient complained of back pain. A bone scan showed increased uptake in T9 vertebra, rib 8 and rib 6 costovertebral junction. CT scan confirmed a lytic lesion on T9 vertebra encroaching the foramen with no cord compression. Palliative radiation (2000 cGy) was administered. The following week, the patient presented with mental confusion secondary to hypercalcemia (ionized Ca⁺⁺=1.46; normal: 1.2-1.35 mmol/L), and finally expired the following month due to septicemia.

Discussion

Hairy cell leukemia is a lymphoproliferative disorder of the B lymphoid system. The last decade has seen a dramatic improvement in the management and overall prognosis of HCL, but concern has emerged with regard to the incidence of second malignancy. Most of these second neoplasms have been solid tumors and few reports of lymphoid malignancies exist. An estimated incidence of 8.7% of second cancers has been reported in HCL patients,² and a possible role of IFN- α in their pathogenesis has also been reported.³

Our cases were treated with IFN- α and 2-CDA, and achieved morphological as well as clinical remission. From the time of diagnosis of HCL to the diagnosis of a second cancer was three to four years. After the diagnosis of the second malignancy, the median survival of such patients was eight months. Previously, the high incidence of second neoplasms in patients with HCL had been attributed to the chemotherapeutic agents causing a worsening of immunological defects which may allow clonal mutation and hence development of second cancer.⁴ There is also a possibility of IFN- α therapy having some direct oncogenic defect, evidenced by a significant decrease in CD4 helper cells in one of our patients.³ An incidence of 19% has been reported in association with IFN.³ Previous investigators have postulated that IFN- α might induce chromosomal change, or permit clones with unusual karyotypes to gain a proliferative advantage.³ On the other hand, Pawson et al. reviewed a larger series of 200 patients with HCL, and found second malignancies in eight cases (4.0%), all but one of whom had received IFN.⁵ However, when compared to age- and sex-matched population data, this represents no increase in relative risk of second cancer in patients with HCL and provides no evidence of a role of IFN in the pathogenesis of these second malignancies. Similarly, Kurzrock et al. found no excess of malignancy among patients treated with IFN- α , 2-CDA or deoxycoformycin (DCF), and hence concluded no association with therapy.⁶ In general, the second neoplasms behave aggressively. The median survival after diagnosis of the second neoplasm

previously reported was only 8.8 months,² similar to what we found in our present cases.

In summary, the possible mechanisms to explain the development of second or even tertiary cancers in patients treated for HCL include: presence of cell-mediated immune deficits⁴; the expression of proto-oncogenes by such patients leading to the transformation and development of second tumors expressing the same proto-oncogenes⁷; the immunological deficits produced by the treatment modalities including splenectomy⁸; direct oncogenic defect of agents like IFN- α ³; old age further contributing to immune dysfunction⁹; possibility of genetic components; shared etiological factors and environmental factors; and last but not the least, the observed increase in the incidence of second neoplasm in this group of patients who are immunocompromised because of HCL and thus prone to develop second tumors. If this is the case, then the frequency of second neoplasms in patients with HCL may be even greater in the future with continued improvements in therapy.

Most previously reported second tumors in patients with HCL are hematological malignancies and adenocarcinomas of the lung, breast, stomach, kidney, cervix, prostate and colon. Our cases indicate that head and neck neoplasms (squamous cell carcinoma) should also be added to the list, particularly in those groups of patients who have previously been treated with such chemotherapeutic agents. Therefore, physicians taking care of patients with HCL need to remain vigilant for second primary tumors. Since HCL is a well-defined clinicopathologic entity, patients with HCL who exhibit unusual features of the disease should be investigated further for the presence of second malignancies.

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Can Residents Conduct a Journal Club In a Better Way?

To the Editor: Journal club presentation of a selected scientific article is a regular feature of any good postgraduate training program. As there is no formal teaching for good journal club presentation, most residents follow the IMRAD style from the text of the paper. They end up writing many pages of transparencies, with some copying the entire printed information in their projections. The journal club should not only be a presentation of the article, but a critical review of the same. The goal is to eliminate irrelevant information, detect deficiencies and summarize the important findings of the paper in a limited time span. The following are a few suggestions that might be of help in making journal club presentation easy and objective.

Selection

The selection of the article should be based on the target audience. A multi-center randomized control clinical study is preferable. Remember that the time for presentation should not exceed 20 minutes.

Title

Check for errors. Some examples of incorrect titles: *HUS in the New Millennium*. What is HUS? Abbreviations are best avoided. Why millennium? Is it such a long study? *Improved Prognosis in Heart Failure Due to Captopril*. Was heart failure caused by captopril or was prognosis improved by its use?

Authorship

- Who is the primary author? A renowned person as author who has done previous work on the same

subject gives the paper a higher rating. However this is not a major merit and should not be taken as the sole criteria for selection.

- Where was the study conducted? Great Ormond Street Hospital, Harvard University or Yale, Karolinska Institute? The reliability and validity are more pronounced when the study was conducted in a reputed institution.
- Submitted, accepted, published (time lapse): A short time between the time of study and publication will rate the paper higher. However, for highly rated journals, a long time lapse is common.

Materials and Methods

What were the inclusion and exclusion criteria? Types/designs of study (pilot, cross-sectional, randomized, blinded, prospective, clinical trial) should be appropriately chosen and described. Detailed description of the general procedure is also required.

Results

- No illusions should be created by graphic presentations. There should not be repetition of data in tabulated form if it has already been presented in the graphic form.
- Numbers of illustrations in tabulated form or figures should be pertinent to the study.
- The method of statistical analysis should be appropriate to the study.

Discussion

The positive and negative points should be highlighted. Were there any flaws or pitfalls? What was the significance and clinical application of the study?

Conclusion

Were the conclusions valid, reliable and drawn from the results?

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