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Info Medicus

The essence of medical practice

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EDITORIAL

Dear Doctor,

Happy New Year

Welcome to our first issue of 2019.

In this issue, we focused on some interesting features like- Febrile seizure; Facts about lung cancer; Cannula insertion technique; A case of splenic pregnancy and Overview of breast cancers.

Febrile seizure can be frightening for parents but are not harmful to the child and usually stop after a few minutes. Keeping this in mind we have emphasized this topic in Health care section. Cannula insertion at times can be a challenging. We all should be aware of the proper ways of inserting a cannula for preventing spread of infections. So, we have taken up this technique in Essential procedure section.

Breast cancer is the most common cancer in women worldwide both in the developed and developing countries. Keeping in mind about the health of the women we have affirmed this imperative topic as Review article section. Other regular features are there as usual.

On behalf of ACI we wish you healthy, properous and peaceful life.

Thanks and best regards

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Febrile seizure

Febrile seizures are the most common seizures of childhood, occurring in 2% to 5% of children among 6 months to 5 years of age. As defined by the American Academy of Pediatrics (AAP), febrile seizures occur in the absence of intracranial infection, metabolic disturbance, or history of afebrile seizures, and are classified as simple or complex. Simple febrile seizures represent 65% to 90% of febrile seizures and require all of the following features: duration of less than 15 minutes, generalized in nature, a single occurrence in a 24 hour period, and no previous neurologic problems. The most common age of onset is in the second year of life. Febrile seizures are slightly more common in males.

Pathophysiology

Most febrile illnesses associated with febrile seizures are due to common infections such as tonsillitis, upper respiratory infections, and otitis media. Children of preschool age are subject to frequent infections and accompanying high fevers, which in combination with a relatively low seizure threshold, allows for the common occurrence of febrile seizures.

Risk factors

The two most consistently identified risk factors for developing febrile seizures are the height of the temperature and a positive family history in first degree relatives. Risk factors are classified into first febrile seizure and recurrence of febrile seizure (Table-1).

Table-1: Risk factors of febrile seizure

First febrile seizure
• Family history of febrile seizures
• Neonatal discharge ≥ 28 days
• Delayed development
• Low serum sodium
• Very high fever
• Child care attendance
Recurrence of febrile seizure
• Young age
• Short duration of fever before the initial seizure
• Relatively lower fever at the time of the initial seizure
• Possible family history of afebrile seizure
• Family history of febrile seizures

First febrile seizure

In studies comparing children who have febrile seizures with febrile controls, a higher temperature was a risk factor for the development of a febrile seizure, as was a history of febrile seizures in a close relative. In a similar study in which both febrile and afebrile control children were examined, a family history of febrile seizures, neonatal discharge 28 days or later, parental report of slow development, and child care attendance were risk factors for febrile seizures. Another recent study found a correlation between low serum sodium levels and risk for developing febrile seizure.

Recurrence of febrile seizure

After the first febrile seizure, approximately 33% of children will experience one or more recurrences, and about 9% of children who have febrile seizures will have three or more. The younger the child when the first febrile seizure occurs, the greater the likelihood of recurrence. Most recurrences (75%) happen within 1 year. A recent study has shown an increased risk of recurrence to be associated with a shorter duration of fever before the initial febrile seizure and a lower temperature. Family history of febrile seizures is another reported risk factor for recurrence. A family history of afebrile seizures has been reported as a risk factor for recurrence in some studies, but not in others. "Complex" febrile seizure are not more likely to be followed by recurrences. Young age of onset and a family history of febrile seizure are the strongest and most consistent predictors of recurrence.

Diagnosis

Febrile seizures usually occur early in the course of a febrile illness, often as the first sign. It commonly has been thought that the rate of increase of the fever is an important trigger, but there are no data to support the importance of this factor over the height of the fever. The seizure may be of any type, but the most common is tonic-clonic seizure. Initially there may be a cry, followed by loss of consciousness and muscular rigidity. During this tonic phase, there may be apnea and incontinence. This is followed by the clonic phase of repetitive, rhythmic jerking movements and then by post-ictal lethargy or sleep.

Evaluation: Children should be promptly evaluated after an initial seizure. Most parents of patients with febrile seizure seek medical care within an hour of the seizure, but after resolution of the seizure and return of the patient to full alertness. The initial evaluation should focus on determining the source of the fever. History taking should include documentation of any family history of febrile seizure or epilepsy, status of immunizations, recent antibiotic use, duration of the seizure, any prolonged postictal phase, and any focal symptoms. On physical examination, attention should be given to the presence of meningeal signs and the child's level of consciousness. To begin, one must consider whether there is an infection of the CNS in the form of meningitis or encephalitis, particularly in younger infants in whom the signs can be more subtle. Therefore, the important issue for evaluation is whether a lumbar puncture is necessary to exclude meningitis. If meningitis is excluded, the next step is to consider what tests are needed to determine the cause of the febrile illness. Finally, consider whether there is a structural CNS abnormality that predisposed the child to having a seizure.

Lumbar puncture: A lumbar puncture (LP) is indicated if there is any clinical suspicion of meningitis. The presence of a source of infection such as otitis media does not rule out meningitis, and if the infant has been taking antibiotics, partially treated meningitis should be suspected and an lumbar puncture performed. In infants younger than 12 months, performance of a lumbar puncture is strongly advised, because the clinical signs and symptoms associated with meningitis may be minimal or absent in this age group. In a child between 12 and 18 months of age, a lumbar puncture should be considered, because clinical signs and symptoms of meningitis may be subtle. In a child older than 18 months, although a lumbar puncture is not routinely warranted, it is recommended in the presence of meningeal signs and symptoms that is neck stiffness and positive kernig and brudzinski signs. In infants and children who have had febrile seizure and have received prior antibiotic treatment, clinicians should be aware that treatment might mask the signs and symptoms of meningitis.

Electroencephalography (EEG): The reported incidence of EEG abnormalities in children with febrile seizure varies from 2% to 86%. This wide range may be due to variable ages of the patients, variable criteria for selection of cases, differences in the definition of abnormalities and variations in the time of EEG recording after seizures. The AAP stated that EEG should not be a part of the routine evaluation in neurologically healthy children with a simple febrile seizure. However, this statement did not include patients with complex febrile seizure.

Treatment

Treatment is acute rescue therapy for prolonged febrile seizure. Antipyretics are not proven to reduce the recurrence risk for febrile seizures. Some evidence shows that both intermittent therapy with oral or rectal diazepam and continuous prophylaxis with oral phenobarbital or valproate are effective in reducing the risk of recurrence, but there is no evidence that these medications reduce the risk of subsequent epilepsy. Vaccine induced febrile seizures is a rare event that does not lead to deleterious outcomes, but could affect patient and physician attitudes toward the safety of vaccination.

References: *1. Am. Fam. Phy., 15 January 2012, Vol. 85, N. 2:149-153*
2. Pediatrics in Review, January 1997, Vol.18, Issue 1
3. Ped. Ann., December 2013, Vol. 42, N. 12:249-254
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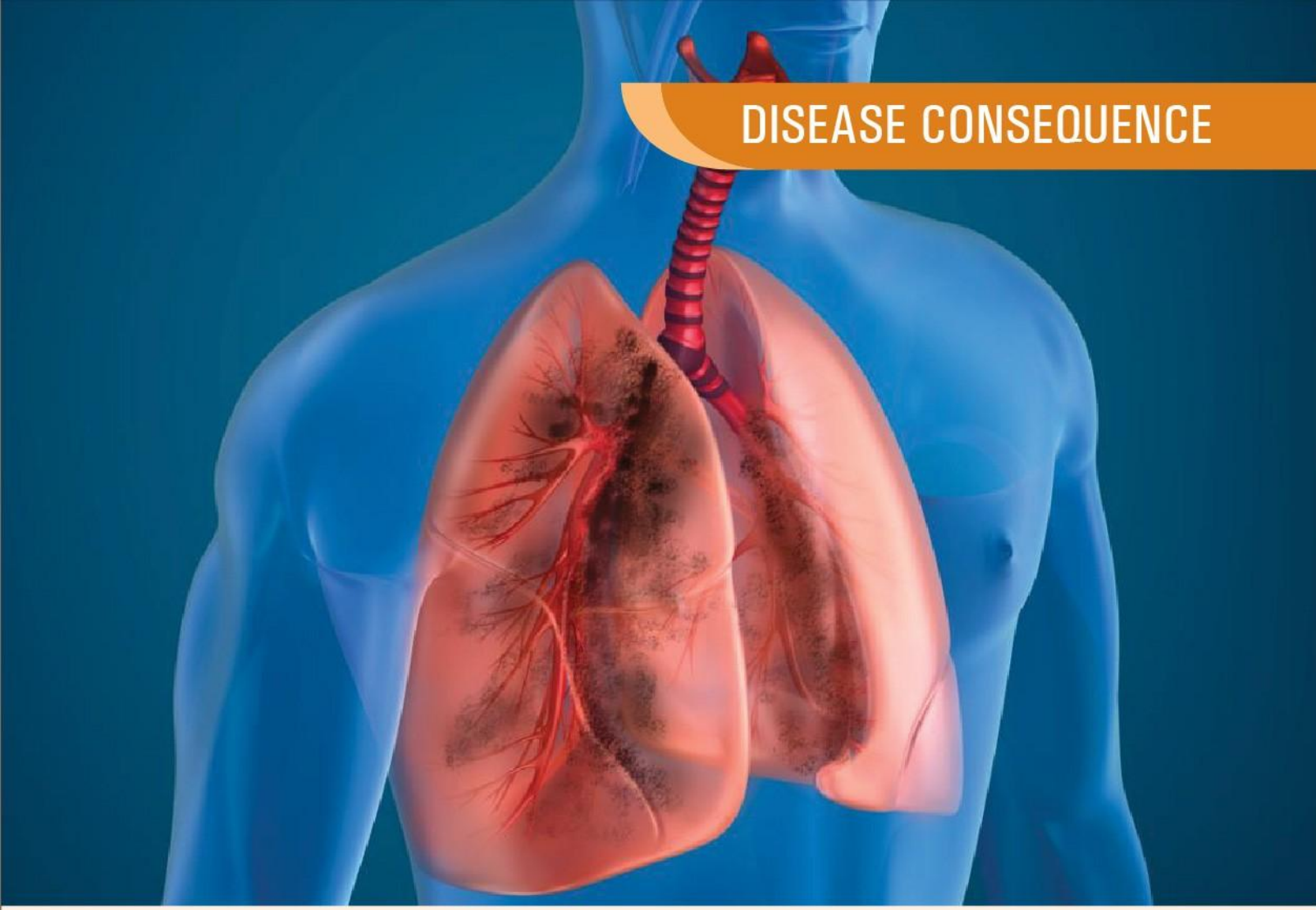
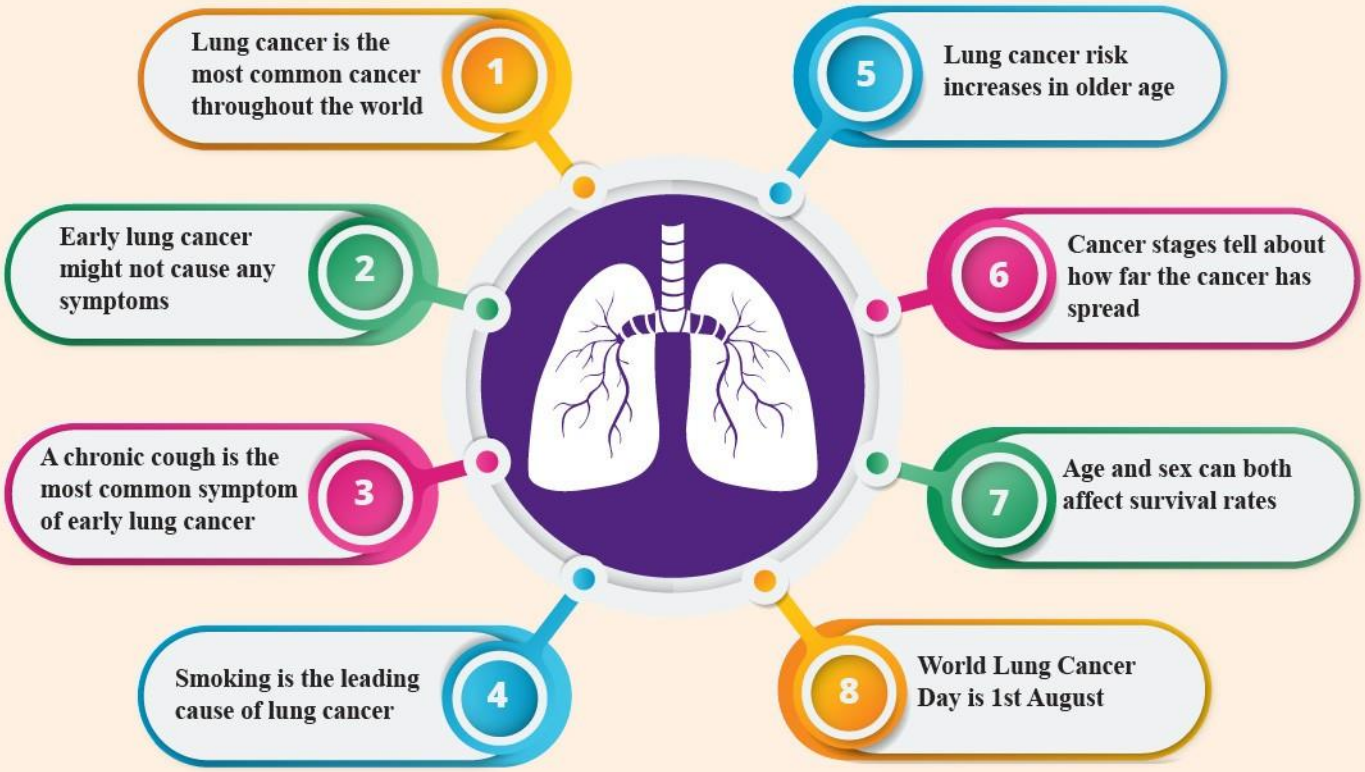


Facts about lung cancer



Cannula insertion technique

Introduction

A cannula is a flexible tube containing a needle which may be inserted into a peripheral vein. Peripheral cannulation provides access for the purpose of intravenous hydration, feeding, and administration of medication and blood products. However, there are some technique and preparation to complete the procedure safely. The basic procedure involves gathering appropriate materials and properly preparing the insertion site, inserting the needle and performing appropriate maintenance and cleanup after the cannula is inserted. Peripheral intravenous cannulation is required in a broad range of clinical applications, including intravenous drug administration, intravenous hydration, and transfusions of blood or blood components, as well as during surgery, during emergency care, and in other situations in which direct access to the bloodstream is needed. Relative contraindications to insertion of a peripheral catheter at a specific site in the body may include infection, phlebitis, sclerosed veins, previous intravenous infiltration, burns or traumatic injury proximal to the insertion site, arteriovenous fistula in an extremity, and surgical procedures affecting an extremity.

Equipment

Preparing to insert a cannula

Cannulation requires some basic preparation and precaution. The materials required are non sterile gloves, tourniquet, antiseptic solution, syringe with needle of appropriate gauge, venous access device, transparent dressing, paper tape and sharps container.

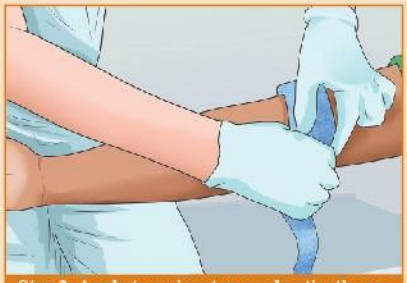
Choose the size of the cannula

There are large and small size gauge needle. Large sized needles actually have a smaller number, so a 14 gauge is large, while a 22 gauge is small.

Procedure

Step 1: Wash hands properly and use gloves

A thorough and proper hygiene practice should be followed before coming into contact with a patient. It is important to keep the risk of the patient getting infection to a minimum while inserting a cannula by washing the hands thoroughly and putting on gloves.

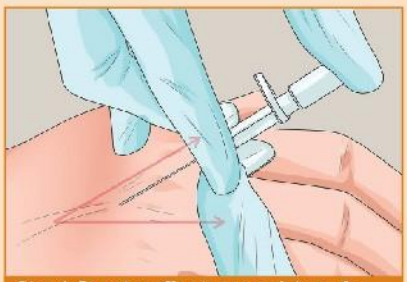


Step 2: Apply tourniquet around patient's arm

In most cases, the patient's non dominant arm is preferable. The tourniquet should be placed on the arm just above the cannulation site. It should be tighten appropriately, so that the patient's veins are highlighted.

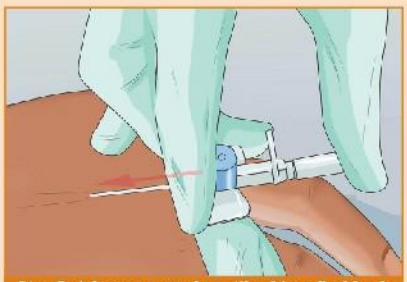
Step 3: Clean skin with antiseptic solution

The skin should be cleaned for cannulation using an antiseptic solution. The antiseptic should be applied to the site with friction for 30 to 60 seconds and then the site should be allowed to air. This will help to prevent the risk of infection.



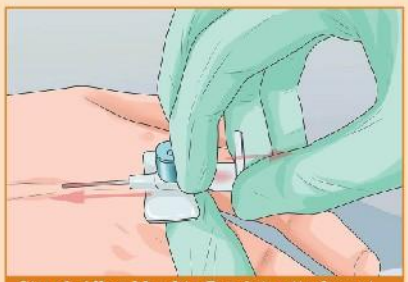
Step 4: Insert needle at appropriate angle

The cannula needle should be inserted at an appropriate angle. For a superficial vein a small cannula with a gauge of 22 to 24 should be used and inserted at an angle of 10° to 25°. For a deeper vein a larger cannula should be inserted at an angle of 30° to 45°.



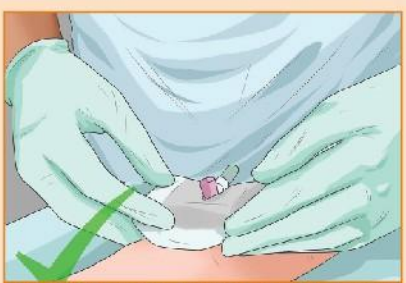
Step 5: Advance cannula until achieve flashback

The cannula should be hold in the front of its wings with the pointer and middle finger and at the back with the thumb. It should be advanced slowly into the skin until blood enters the base of the cannula. This is called a flashback and it signals the correct entrance to a vein.



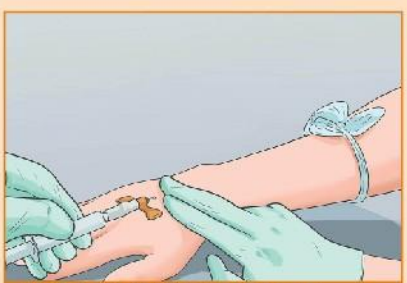
Step 6: Allow blood to flow into attachment

The blood should flow into an attachment. The tourniquet should be removed from the patient's arm. The needle should be removed from the base of the cannula leaving the plastic component in sight. The blood allowed to flow into the base of the cannula.



Step 7: Secure cannula with appropriate dressing

If the cannula needs to stay in the vein then it should be secured. A transparent dressing and tape or a specialized dressing that comes with the cannula should be used to secure the venous access device to the skin.



Step 8: Inspect and clean the cannula

During cleaning the cannula, firstly the syringe should be pulled back to withdraw a little blood. This will confirm that the cannula is still in place inside the vein. Then the cannula should be flushed using a flushing solution such as normal saline or heparin.

Step 9: Dispose needle in a sharps container

All the needles should be disposed in a sharp container to reduce the risk of a needle stick. All other waste products should be disposed appropriately.

References: *1. N. E. J. M., 20 Nov 2008, 359 (7)*
2. www.wikihow.com
3. www.gosh.nhs.uk

A case of splenic pregnancy

Ectopic pregnancy is defined as implantation of a fertilized ovum in tissue other than the endometrium. Its incidence is 19.7 per 1000 pregnancies. The most common site of ectopic implantation is ampulla of the fallopian tube, accounting for more than 92% of all ectopics. Abdominal pregnancies account for approximately 1.4% of all ectopic pregnancies and occur with direct implantation onto the peritoneal surface. Abdominal pregnancies have been described in extrapelvic organs like omentum, liver, spleen, small and large intestine. The spleen is one of the rare sites for ectopic gestation, and to our knowledge, only ten cases of primary splenic pregnancy have been documented in literature till date. This case report is of a 19-year-old patient who presented with abdominal pain, pregnancy test positive and haemoperitoneum and was taken up for exploratory laparotomy, and splenic pregnancy was diagnosed intraoperatively.

Case

A 19 year old married woman suffered from abdominal pain and fullness since two days. She had regular menstrual cycles. Her last menstruation was 4 weeks prior. An abdominal ultrasound was done at the peripheral hospital, which revealed a normal uterus, normal bilateral fallopian tubes and ovaries, and moderate to severe haemoperitoneum and all abdominal organs within normal limits. A urine pregnancy test done there was positive. On clinical examination, the patient had moderate pallor, pulse of 120 beats per minute and blood pressure of 90/60 mm Hg. On abdominal examination, diffuse abdominal tenderness was present with abdominal distension. Gynaecological examination revealed a normal cervix, minimal brownish vaginal discharge, normal-sized uterus with no adnexal tenderness. Her serum beta human chorionic gonadotropin level was sent on admission. Since the patient was haemodynamically unstable, pregnancy test was positive along with haemoperitoneum, she was taken up for an emergency exploratory laparotomy under general anaesthesia, with clinical suspicion of a ruptured ectopic pregnancy, probably undiagnosed radiologically. Pre-operatively, her haemoglobin value was found to be 7.2 g/dl. All other routine investigations were within normal limits. The abdomen was opened with a transverse 4 to 5 cm long suprapubic incision. Intraoperatively, haemoperitoneum of approximately 1200 cc was noted. The uterus, bilateral fallopian tubes and ovaries were normal, and no evidence of a tubal or ovarian ectopic pregnancy was found.

Meanwhile, her serum beta HCG value sent on admission was found to be more than 10,000 mIU/ml. The abdominal cavity was then further inspected by extending our incision upwards in the midline. A careful exploration of the abdomen revealed fresh blood clots and blood collection in the left paracolic area, which was traced to originate from the spleen. The spleen on its superolateral surface showed attachment of irregular soft, chorionic villous or trophoblast like tissue, approximately 3 × 2 cm in size. Active bleeding from the superolateral surface of the spleen was present (Figure-1).

The adherent tissue was separated from the splenic surface, and a splenorrhaphy was performed by our surgery faculty, conserving the spleen. The tissue retrieved was sent for histopathological examination. The abdomen was closed in layers once haemostasis was ensured. Two drains were kept intra-abdominally one each in the splenic and pelvic areas, to allow any collection to drain out. Following closure, a uterine dilation and curettage was performed and tissue was sent for histopathology for any evidence of intrauterine pregnancy.

The patient received three packed cell transfusions intraoperatively and one post-operatively. For the first 48 hours, she was monitored under close supervision. Higher antibiotics and analgesics were administered to the patient. Her postoperative period was uneventful. Value of serum beta HCG repeated on fourth post-operative day was 802.4 mIU/ml with all vital parameters showing considerable improvement, and haemoglobin level repeated was 9.8 g/dl. Both drains had minimal collection and were removed on the fifth postoperative day. After 1 week, the beta HCG value decreased to 39.6 mIU/ml. The patient recovered uneventfully and was discharged on the 11th postoperative day.

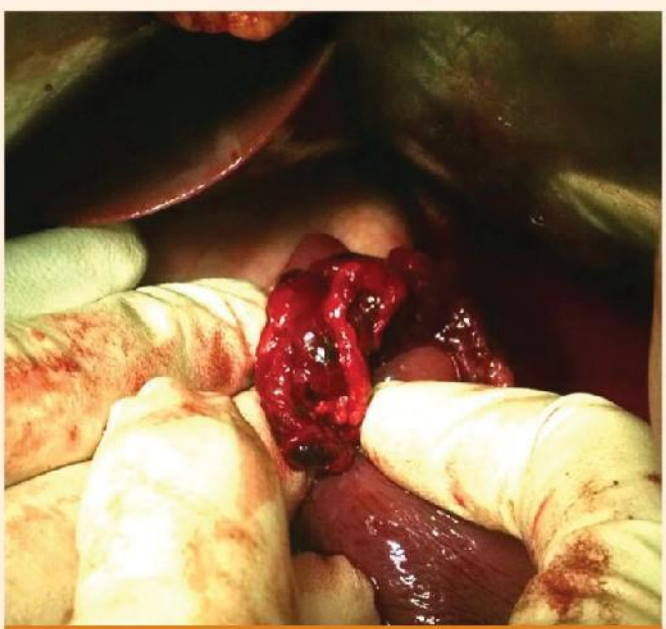


Figure-1: Mass attached to the superolateral splenic surface with bleeding from its site of attachment

Histopathological findings

Histopathological examination of tissue retrieved from spleen showed haemorrhagic areas in splenic tissue, with intervening chorionic villous tissue. Histopathology of endometrial tissue revealed normal endometrium negative for any products of conception.

Discussion

Abdominal pregnancy is an implantation in the peritoneal cavity exclusive of tubal, ovarian or intraligamentous implantations. It may be primary or secondary. Estimated incidence ranges from 1 in 10,000 to 1 in 25,000 live births. It is associated with high morbidity and mortality, with the risk for death 7 to 8 times greater than tubal ectopic pregnancy and 50 times greater than intrauterine pregnancy. Studdiford's criteria for diagnosis of primary abdominal pregnancy are presence of normal tubes and ovaries with no evidence of recent or past pregnancy, no evidence of uteroplacental fistula, the presence of a pregnancy related exclusively to the peritoneal surface and early enough to eliminate the possibility of secondary implantation after primary tubal nidation.

The sites of abdominal pregnancy are the pouch of Douglas, posterior uterine wall and extrapelvic structures such as small and large intestine, omentum, liver and spleen. Incidence of splenic pregnancy is very rare. The spleen is a relatively more favourable organ for implantation since it is a flat organ, rich in blood flow and easily reached by the fertilized ovum in the supine position. However, none of the anatomic sites described above, including the spleen, can accommodate placental attachment or a growing embryo; therefore, rupture and a massive haemorrhage may very likely occur if left untreated. Primary splenic pregnancy tends to present earlier than other abdominal pregnancies, mostly presenting with acute abdomen and haemoperitoneum occurring at 6 to 8 weeks of gestation. Because of the abundant blood supplies, splenic ectopic pregnancy may have massive peritoneal bleeding and the patient may present with hypovolemic shock.

Summary

This case is an intraoperative detection of pregnancy on the spleen, with no abnormalities of the uterus and fallopian tubes and no evidence of pregnancy other than the spleen. Recognition of this rare form of ectopic gestation is of considerable importance because of the risk of a life threatening peritoneal haemorrhage necessitating emergency surgical intervention and even splenectomy.

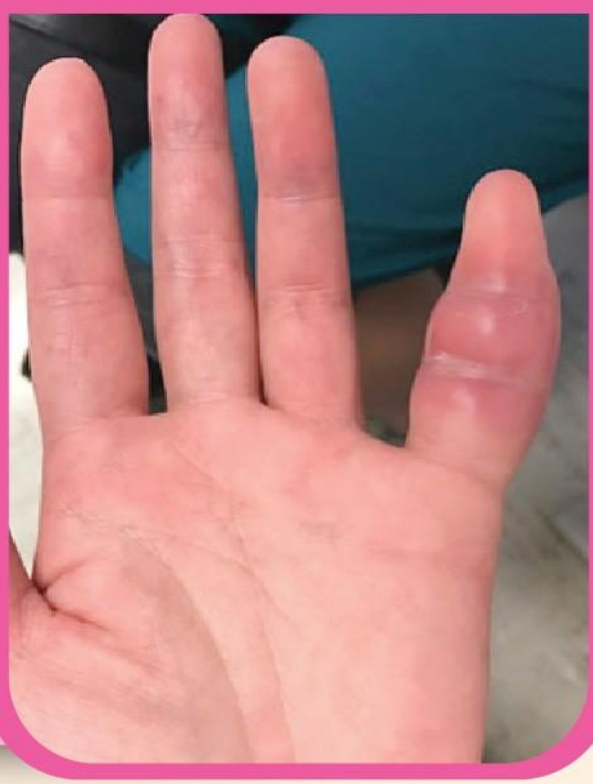
Reference: J. Obs. and Gyn. Ind., August 2017, Vol. 67, N. 4

Nail changes during chemotherapy

A 42 year man who was undergoing treatment for non-Hodgkin's lymphoma presented to the oncology clinic with changes in his fingernails. Five months earlier, he had presented with gastric outlet obstruction and had received a diagnosis of high grade B-cell non-Hodgkin's lymphoma. He then completed four cycles of chemotherapy, which had included rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin. Physical examination showed diffuse, dark brown discoloration of his fingernails and two types of transverse white lines that were not palpable. The serum albumin level was 2.5 g per deciliter (reference range 3.5 to 5.0). The opaque appearing transverse lines on the fingernails are called Mees' lines (true leukonychia), and the more translucent appearing lines are called Muehrcke's lines (apparent leukonychia). Mees' lines develop as a result of injury to the nail matrix, whereas Muehrcke's lines are related to abnormal nail bed vasculature. Therefore, Mees' lines do not diminish with compression of the nail plate, and Muehrcke's lines do. Approximately 6 months after the completion of chemotherapy, the fingernail changes resolved completely.

Reference: N. Eng. J. Med., 18 October 2018, Vol. 379, N. 16

Tuberculosis of the finger



A 42 year woman presented with a 1 week history of swelling and pain in the fifth finger of her left hand. She reported no related trauma. Physical examination of the affected finger revealed soft tissue swelling, with erythema and warmth, that was most prominent between the proximal and distal interphalangeal joints, sparing the fingertip. Radiography and magnetic resonance imaging revealed swelling of soft tissue but no bony abnormalities. Examination of a biopsy specimen of the deep dermis after fite staining revealed numerous acid fast bacilli. Culture of a tissue sample grew *Mycobacterium tuberculosis.* Findings on radiography of the chest were normal. The patient had undergone a purified protein derivative skin test before starting immunosuppressive therapy; the result was negative. Further investigation revealed that the patient's husband had active pulmonary tuberculosis after coming from China. Although infection of the finger is a rare extrapulmonary manifestation of tuberculosis, it is an important consideration in immunosuppressed patients. This patient was treated with a four drug antituberculosis regimen for a total of 9 months and had complete resolution of her symptoms.

Reference: N. Eng. J. Med., 20 September 2018, Vol. 379, N. 12

Overview of breast cancer

Introduction

Breast cancer is the most common cancer and also the leading cause of cancer mortality in women worldwide. Approximately 1.38 million new breast cancer cases were diagnosed in 2008 with almost half of all breast cancer cases and nearly 60% of deaths occurring in lower income countries. There is a large variation in breast cancer survival rates around the world, with an estimated 5 years survival of 80% in high income countries to below 40% for low income countries. According to the estimation by the National Institute of Cancer Research and Hospital Dhaka, Bangladesh in 2014, approximately 26% female patients battle against breast cancer. Women who have one first degree relative (mother, sister, or daughter) with a history of breast cancer are nearly twice as likely to develop breast cancer and to some extent, the ovarian cancer. Treatment options for breast cancer vary depending on the stage at which the cancer is diagnosed. Surgery and radiotherapy are commonly used to treat women with early stage breast cancer. Chemotherapy and hormonal therapies are frequently used to treat patients with more advanced forms of the disease. This guide provides an overview of breast cancer including risk factors, symptoms, diagnosis, incidence and treatment options.

Anatomy of healthy breast

The female breast is mostly made up of a collection of fat cells called adipose tissue. A healthy female breast (Figure-1) is made up of 12-20 sections called lobes. Each of these lobes is made up of many smaller lobules, the gland that produces milk in nursing women. Both the lobes and lobules are connected by ducts, which act as stems or tubes to carry the milk to the nipple. Within the adipose tissue is a network of ligaments, fibrous connective tissue, nerves, lymph vessels, lymph nodes, and blood vessels.

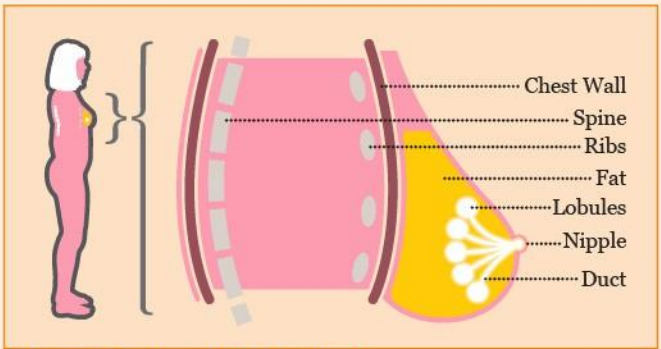


Figure-1: Anatomy of healthy breast

Classification

Breast cancer is an abnormal growth of cells that normally line the ducts and the lobules. Breast cancer is classified by whether the cancer started in the ducts or lobules, whether the cells have "invaded" (grown or spread) through the duct or lobule, and the way the cancer cells look under a microscope. Breast cancers are broadly grouped into those that are still in the breast lobules or ducts (referred to as "noninvasive" or "carcinoma in situ") and those that have spread beyond the walls of the ducts or lobules (referred to as "infiltrating" or "invasive").

Carcinoma in situ

Carcinoma is another word for cancer and carcinoma in situ (CIS) means that the cancer is a very early cancer and it is still confined to the ducts or lobules where it started. It has not spread into surrounding fatty tissues in the breast or to other organs in the body. There are 2 types of breast carcinoma in situ:

Lobular carcinoma in situ (LCIS): Also called lobular neoplasia. It begins in the lobules, but has not grown through the lobule walls. Breast cancer specialists do not think that LCIS itself becomes an invasive cancer, but women with this condition do run a higher risk of developing an invasive cancer in either breast.

Ductal carcinoma in situ (DCIS): This is the most common type of noninvasive breast cancer. In DCIS, cancer cells inside the ducts do not spread through the walls of the ducts into the fatty tissue of the breast. DCIS is treated with surgery and sometimes radiation, which are usually curative. If not treated, DCIS may grow and become an invasive cancer.

Invasive breast cancers

Invasive cancer describe those cancers that have started to grow and have spread beyond the ducts or lobules. These cancers are divided into different types of invasive breast cancer depending on how the cancer cells look under the microscope. They are also grouped according to how closely they look like normal cells.

Invasive ductal carcinoma (IDC): It is also called infiltrating ductal carcinoma. The cancer starts in a milk passage, or duct, of the breast, but then the cancer cells break through the wall of the duct and spread into the fatty tissue. Cancer cells can then spread into lymphatic channels or blood vessels of the breast and to other parts of the body. About 80% of all breast cancers are invasive ductal carcinoma.

Invasive lobular carcinoma (ILC): It is also called infiltrating lobular carcinoma. This type of cancer starts in the milk producing glands. Like IDC, this cancer can spread beyond the breast to other parts of the body. About 10% to 15% of invasive breast cancers are invasive lobular carcinomas.

Mixed tumors: Mixed tumors describe those that contain a variety of cell types, such as invasive ductal combined with invasive lobular breast cancer. With this type, the tumor is usually treated as if it were an invasive ductal cancer.

Medullary cancer: This special type of infiltrating ductal cancer has a fairly well defined boundary between tumor tissue and normal breast tissue. It also has a number of special features including the presence of immune system cells at the edges of the tumor. It accounts for about 5% of all breast cancer. It can be difficult to distinguish medullary breast cancer from the more common invasive ductal breast cancer.

Metaplastic tumors: Metaplastic tumors are a very rare type of invasive ductal cancer. These tumors include cells that are normally not found in the breast, such as cells that look like skin cells (squamous cells) or cells that make bone. These tumors are treated similarly to invasive ductal cancer.

Inflammatory breast cancer (IBC): Inflammatory breast cancer is a special type of breast cancer in which the cancer cells have spread to the lymph channels in the skin of the breast. Inflammatory breast cancer accounts for about 1% to 3% of all breast cancers. Inflammatory breast cancer has a higher chance of spreading and a worse outlook than typical invasive ductal or lobular cancer.

Colloid carcinoma: This rare type of invasive ductal breast cancer, also called mucinous carcinoma, is formed by mucus producing cancer cells.

Tubular carcinoma: Tubular carcinoma is a special type of invasive ductal breast carcinoma. About 2% of all breast cancers are tubular carcinomas. Women with this type of breast cancer have a better outlook because the cancer is less likely to spread outside the breast than invasive lobular or invasive ductal cancers of the same size.

Risk factors

Age, reproductive factors, personal or family history of breast disease, genetic pre-disposition and environmental factors have been associated with an increased risk for the development of female breast cancer.

Age: Breast cancer is very uncommon before 20 years of age, but the incidence gradually increases with age and by the age of 90 years, one fifth of women are affected. It is also believed that the age at menarche and menopause contribute to the duration of exposure to the carcinogenic effects of the gonadal (sex) hormones.

Genetic factors: Breast cancer is more common in women with a family history compared to the general population. About 5% of breast cancers are related to a specific mutation. Also, 12% of women with this disease have one affected family member and 1% of the patients have one or more relatives affected. It is concluded that women with one or more first degree relatives affected with breast cancer have higher breast cancer risk than those who do not.

Diet: These are thought to play a role in the etiology of breast cancer and there is a link between diets low in phytoestrogens and this disease. Furthermore, well cooked meat and diets rich in fats are associated with increased incidence of breast cancer, diets containing 35% to 40% of fat in calories. This is because high fat diets are rich in cholesterol which is a precursor in the synthesis of estrogens and other steroid hormones.

Lifestyle and physical activity: Along with diet, exercise can interfere with plasma levels of hormones which may influence breast cancer development. These two factors separately or in combination influence the body weight and obesity increases the risk of breast cancer in post-menopausal women. Breast cancer risk is particularly evident among obese women who don't use hormone replacement therapy.

Mammographic density: This is well documented risk factor for the development of breast cancer during and after the reproductive ages. Women with > 75% increased breast density on mammography have up to a five fold increased risk over those with < 5% increased breast density. Women with a tumor size of > 1 cm were more likely to have dense breasts compared with those with a tumor size < 1 cm, and that lymph node status, lymphatic and/or vascular invasion were positively associated with breast density.

Benign breast disease: A previous history of benign breast disease like fibrocystic disease and fibroadenoma are known to increase the risk of breast cancer. Fibroadenosis with severe dysplasia and epitheliosis is considered to be pre-malignant even though not all cases progress to cancer.

Molecular genetics of breast cancer: 5% to 10% of all breast cancers arise from germ line mutations in high penetrance breast cancer susceptibility genes such as BRCA1, BRCA2, p53 and PTEN, and confer a high individual risk for developing hereditary breast cancer. The BRCA1 gene is located on the long arm of chromosome 17, while BRCA2 is located on the long arm of chromosome 13. Gene positive patients have an 80% risk of developing breast cancer especially in the pre-menopausal age group. BRCA1 and BRCA2 predispose a woman to breast cancer in only 5% to 10% of the total number of breast cancers.

Grade and staging

Grade: The grade of a breast cancer is a prognostic factor and is representative of the 'aggressive potential' of the tumor. In a broad generalization, 'low grade' cancers tend to be less aggressive than 'high grade' cancers. Determining the grade is very important, and because it helps to treat the patients. However, tumors are graded between 1 and 3 (Figure-2).

Grade 1 - The cancer cells look small and uniform like normal cells, and are usually slow growing compared to other grades of breast cancer.

Grade 2 - The cancer cells are slightly bigger than normal cells, varying in shape and are growing faster than normal cells.

Grade 3 - The cancer cells look different to normal cells, and are usually faster growing than normal cell.

Figure-2: Grade of tumor

Staging: Staging is used to assess the size of a tumor, whether it has spread and how far it has spread. Understanding the stage of the cancer helps to predict the likely outcome and design a treatment plan for individual patients. The main method used for defining the stage of a cancer is the TNM (Tumor, Nodes, Metastasis) system. The TNM system is often used to categories cancers into four stages (Figure-3).

Stage 1 - Usually means that a cancer is relatively small and contained within the breast.

Stage 2 - Usually means the cancer has not started to spread into surrounding tissue but the tumor is larger than in stage 1. Sometimes stage 2 means that cancer cells have spread into lymph nodes close to the tumor.

Stage 3 - Usually means the cancer is larger. It may have started to spread into surrounding tissues and there are cancer cells in the lymph nodes in the area.

Stage 4 - Means the cancer has spread from where it started to another body organ. This is also called secondary or metastatic cancer.

There is another classification according to American Joint Commission on Cancer guidelines which is given in Table-1.

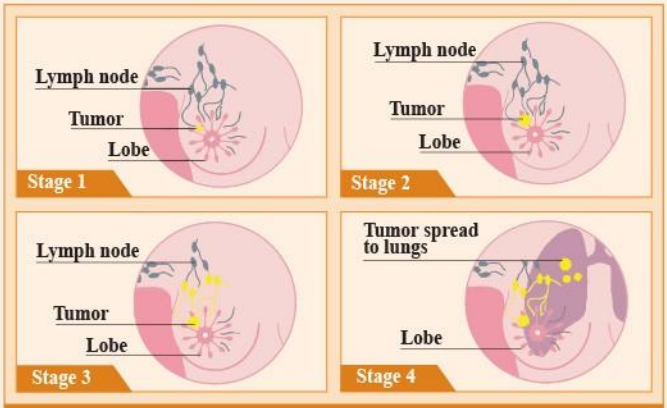


Figure-3: TNM staging of breast cancer

Table-1: American Joint Commission on Cancer guidelines–tumor node metastasis classification

Primary tumor (T)

- TX: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- Tis: Carcinoma *in situ*
- Tis (DCIS): Ductal carcinoma *in situ*
- Tis (LCIS): Lobular carcinoma *in situ*
- Tis (Paget's): Paget's disease of the nipple
- T1: Tumor ≤ 20 mm in greatest dimension
- T1mi: Tumor ≤ 1 mm in greatest dimension
- T1a: Tumor > 1 mm but ≤ 5 mm in greatest dimension
- T1b: Tumor > 5 mm but ≤ 10 mm in greatest dimension
- T1c: Tumor > 10 mm but ≤ 20 mm in greatest dimension
- T2: Tumor > 20 mm but ≤ 50 mm in greatest dimension
- T3: Tumor > 50 mm in greatest dimension
- T4: Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules)
- T4a: Extension to the chest wall, not including only pectoralis muscle adherence/invasion
- T4b: Ulceration and/or ipsilateral satellite nodules and/or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma
- T4c: Both T4a and T4b
- T4d: Inflammatory carcinoma

Regional lymph nodes (N)

- NX: Regional lymph nodes cannot be assessed (for example, previously removed)
- N0: No regional lymph node metastases
- N1: Metastases to movable ipsilateral level I, II axillary lymph node(s)
- N2: Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in clinically detected ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases

  Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures
- N2a: Metastases only in clinically detected ipsilateral internal mammary nodes and in the absence of clinically evident level I, II axillary lymph node metastases
- N2b
- N3: Metastases in ipsilateralinfraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
- N3a: Metastases in ipsilateralinfraclavicular lymph node(s)
- N3b: Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
- N3c: Metastases in ipsilateral supraclavicular lymph node(s)

Distant metastases (M)

- M0: No clinical or radiographic evidence of distant metastases
- cM0 (i +): No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumor cells in circulating blood, bone marrow, or other nonregional nodal tissue that are no larger than 0.2 mm in a patient without symptoms or signs of metastases
- M1: Distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm

Screening

Breast self and clinical breast examination

Women are encouraged to perform monthly breast self examination (BSE) to become familiar with their normal anatomy and empower them with regards to their own healthcare. The 2013 National Comprehensive Cancer Network (NCCN) guidelines recommend annual clinical breast examination (CBE) for women of average risk > 40 years of age as well as BSE to develop and exhibit breast self-awareness.

Diagnosis

History and physical examination

The clinical history is directed at assessing cancer risk and establishing the presence or absence of symptoms indicative of breast disease. The patient should be assessed for specific symptoms like breast pain, nipple discharge, malaise, bony pain and weight loss. Physical examination should include a careful visual inspection with the patient sitting upright. Nipple changes, asymmetry and obvious masses should be noted. The skin must be inspected for changes such as, dimpling, erythema, peau d' orange (associated with local advanced or inflammatory breast cancer). After careful inspection and with the patient in the sitting position the cervical, supraclavicular and axillary lymph node basins are palpated for adenopathy. When palpable the size, number and mobility should be ascertained. Palpation of the breast parenchyma itself is performed with the patient supine and the ipsilateral arm placed over the head. The sub areolar (central quadrant) and each quadrant of both breasts is palpated systematically.

Mammography

Mammography remains the mainstay in breast cancer detection. Diagnostic mammograms are performed in women who have a palpable mass or other symptom of breast disease, a history of breast cancer within the preceding 5 years, or have been recalled for additional imaging from an abnormal screening mammogram. Carcinomas present as masses, asymmetries, and calcifications. The shape of masses is described as round, oval, lobular, or irregular, while the margins are identified as circumscribed (with well defined margins), indistinct, and spiculated (with densities radiating from the margins). Calcifications associated with benign disease are generally larger than those seen with malignancy and typically are coarse.

Ultrasound

The current indications for breast ultrasonography include palpable findings abnormalities or suspected abnormalities on mammography or MRI, problems with breast implants, suspected underlying mass in the setting of micro calcifications or architectural distortion on mammography, supplemental screening in women at high risk for breast cancer who are not candidates for or do not have easy access to MRI, and suspected axillary lymphadenopathy.

MRI

Breast MRI has become an integral part of breast cancer diagnosis and management in selected patients. Current indications for breast MRI include evaluation of patients in whom mammographic evaluation is limited by augmentation including silicone and saline implants and silicone injections, determining the extent of disease at the time of initial diagnosis of breast cancer, evaluation of inconclusive findings on clinical examination, mammography, and or ultrasonography, screening of the contralateral breast in selected patients with newly diagnosed breast carcinoma. Other uses of breast MRI include evaluation of response to neoadjuvant chemotherapy with imaging before, during, and or after treatment, and identification of residual disease in patients with positive margins after lumpectomy.

Treatment

Breast cancer treatment options vary depending on the stage of the cancer- its size, position, whether it has spread to other parts of the body and the physical health of the patient. Current treatments for breast cancer include surgery, radiotherapy, chemotherapy and hormonal therapy. These therapies may be used alone or in combination depending on the stage of the disease.

Surgery

This is the main treatment option for patients whose breast cancer has notspread to other parts of the body and is also an option for more advanced stages of the disease. The types of breast cancer surgery differ in the amount of tissue that is removed with the tumor; this depends on the tumor's characteristics, whether it has spread, and the patient's personal feelings. Some of the most common types of surgery include in Table-2.

Table-2: Surgery option of breast cancer

- Breast conserving therapy or 'Lumpectomy' which involves the removal of the cancerous area, the surrounding tissue and in some cases the lymph node, whist aiming to maintain a normal breast appearance after surgery
- 'Partial Mastectomy' or 'Quadrantectomy'; this is where a larger portion of tissue is removed (compared with lumpectomy)
- 'Total Mastectomy', which is performed in an attempt to further cancer prevention. This surgery involves the removal of the entire breast, without the removal of lymph nodes

Surgery can also be followed or preceded by radiotherapy or chemotherapy, either sequentially or in combination.

Radiotherapy

Therapy with radiation is often used in addition to surgery and chemotherapy to reduce the chances of the cancer recurring. It can be given after surgery (known as adjuvant treatment) or in

conjunction with chemotherapy prior to surgery (neoadjuvant therapy) to shrink the tumor. Radiotherapy can also be used without surgery in patients with advanced metastatic breast cancer to help alleviate symptoms. Radiotherapy has an important role in the treatment of breast cancer at every stage. In early stage disease, radiotherapy is an integral part of breast conserving therapy. For patients with more advanced cancers, adjuvant radiotherapy substantially decreases the risk of local recurrence, and also improves the survival among patients with positive axillary lymph nodes. In locally advanced disease often the most common presentation in the limited resource setting, after neoadjuvant systemic therapy, patients require both radiotherapy and modified radical mastectomy in an effort to achieve local control. In addition, radiotherapy is a valuable tool for the palliation of distant metastasis such as bone and brain metastases, as well as palliation for local recurrences.

Chemotherapy

Chemotherapy may be given prior to surgery (neoadjuvant therapy) with the aim of reducing tumor size and the need for extensive surgery or after surgery (adjuvant therapy) to reduce the chances of the cancer coming back. Adjuvant chemotherapy helps eradicate residual local or distant residual microscopic metastatic disease. The addition of taxanes (paclitaxel anddocetaxel) to the standard anthracycline based chemotherapy has been studied extensively and has shown a significant reduction of 17% in the risk of recurrence. When the cancer has spread to other parts of the body (metastatic), chemotherapy may be used to reduce symptoms, improve quality of life and extend survival. Chemotherapy drugs can be given intravenously (directly into the blood), or orally in a tablet. Chemotherapy is typically associated with adverse effects such as fatigue, nausea and diarrhea, this is because of its toxic nature and non-specific mode of action, which means that all cells are attacked. For adjuvant hormonal and chemotherapy for invasive breast cancer vary depending on hormone receptor positivity or negativity.

Hormone therapy

Hormone therapy is often used after surgery (adjuvant therapy) to help reduce the risk of the cancer coming back. Sometimes it is started before surgery (neoadjuvant therapy) as well. It is usually taken for at least 5 years. Hormone therapy can also be used to treat cancer that has come back after treatment or that has spread to other parts of the body. About 2 out of 3 breast cancers are hormone receptor-positive. Their cells have receptors (proteins) that attach to the hormones estrogen (ER-positive cancers) and/or progesterone (PR-positive cancers). For these cancers, high estrogen levels help the cancer cells grow and spread. There are several types of hormone therapy, which use different ways to keep estrogen from helping the cancer grow. Most types of hormone therapy for breast cancer either lower estrogen levels or stop estrogen from acting on breast cancer cells. Two common types of breast cancer hormone therapy are:

- Selective estrogen receptor modulators (SERMs) or drugs that block estrogen receptors
- Aromatase inhibitors or drugs that lowers the estrogen levels

SERMs or drugs that block estrogen receptors (e.g., tamoxifen, toremifene and fulvestrant): These drugs work by stopping estrogen from stimulating breast cancer cells to grow. Tamoxifen stops estrogen from connecting to the cancer cells and telling them to grow and divide. While tamoxifen acts like an anti-estrogen in breast cells, it acts like an estrogen in other tissues, like the uterus and the bones. Because of this, it is called a selective estrogen receptor modulator (SERM).

Aromatase inhibitors or drugs that lower the estrogen levels (e.g., letrozole, anastrozole and exemestane): These breast cancer hormone therapy drugs block estrogen production by binding to the enzyme responsible for producing estrogen (the aromatase enzyme). Once estrogen production is halted, the cancer cells starve from lack of estrogen, which prevents them from growing and dividing. Some hormone treatments work by lowering estrogen levels. Because estrogen encourages hormone receptor-positive breast cancers to grow, lowering the estrogen level can help slow the cancer's growth or help prevent it from coming back.

Hormone inhibitors and blocker options may depend on a person's stage of life.

- Hormone inhibitors are only used in postmenopausal women
- Hormonal therapy may also be called anti-hormone treatment. If pathology tests show that the tumor of breast has estrogen receptor positive and/or progestersone receptor positive, then this therapy may be recommended for after the completion of surgery, chemo therapy, and radiation
- Hormonal therapy keeps breast cancer cells from receiving or using the natural female hormones in the body (estrogen and progesterone) which they need to grow. These therapy also blocks the ability of healthy breast cells to receive hormones that could stimulate breast cancer cells to regrow again in the form of recurrence of the breast cancer within the breast or elsewhere in the body

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Fingerprint drug screen test works on the living and deceased

A revolutionary drug test developed from research carried out at the University of East Anglia (UEA), Norwich, England which can detect four classes of drugs in traces of sweat found in a fingerprint. This technology works on both the living and deceased. This new research published in the Journal of Analytical Toxicology shows how the Intelligent Fingerprinting Drug Screening System enables the detection of amphetamines, cannabis, cocaine and opiates from a single fingerprint sample in just 10 minutes. Unlike conventional screening methods which require the collection of saliva or urine samples, the technique is non-invasive, dignified and non-biohazardous. Its use in coroner mortuaries demonstrates the value of the system, which is also being used in drug rehabilitation centres and workplaces. The technology also works when used by UK coroners to detect drugs in the sweat of fingerprint samples gathered from deceased individuals.

Founded in 2007, Intelligent Fingerprinting is a spin-out company from UEA. The Drug Screening System works by analysing the sweat from a fingerprint sample. Emeritus Prof. David Russell, from UEA's School of Chemistry, was a co-author of the research and is Intelligent Finger printing's Founder and Chief Scientific Officer. He said that the new research highlights how our lateral flow drug screening cartridge can screen rapidly for drug use in individuals using a fingerprint sample with a sample collection time of only 5 seconds and a total analysis time of 10 minutes. He also said that this study also showed how their technology is being used by coroners to assist in gaining early understanding of the possible cause of death, and to inform potential further post-mortem activities or quickly facilitate police investigations. Studies are also underway for its use in airport screening and for offender management applications within prisons and probation services. Intelligent Finger printing's Dr. Paul Yates said that this important research demonstrates how there is sufficient sweat present in a subject's fingerprint, regardless of whether the person is alive or dead, to enable our fingertip based drug screening system to detect the presence of four major drugs of abuse at the same time.

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New drug could sustain oxygen-starved hearts

Researchers from the University of California at San Francisco (UCSF) have developed a novel therapeutic that can deliver oxygen specifically to under-oxygenated tissues, thereby restoring the contractile function of cardiac cells, which is heavily affected under hypoxic conditions. The heart exhibits the highest basal oxygen (O_2) consumption per tissue mass of any organ in the body and is uniquely dependent on aerobic metabolism to sustain contractile function. During acute hypoxic states, the body responds with a compensatory increase in cardiac output that further increases myocardial O_2 demand, predisposing the heart to ischemic stress and myocardial dysfunction. A novel engineered protein derived from the heme-based nitric oxide (NO)/oxygen (H-NOX) family of bacterial proteins as an O_2 delivery biotherapeutic (Omniox-cardiovascular [OMX-CV]) for the hypoxic myocardium. Because of their unique binding characteristics, H-NOX-based variants effectively deliver O_2 to hypoxic tissues, but not those at physiologic O_2 tension. Additionally, H-NOX-based variants exhibit tunable binding that is specific for O_2 with sub physiologic reactivity towards NO, circumventing a significant toxicity exhibited by hemoglobin (Hb) based O_2 carriers (HBOCs).

Researchers conducted a study where they used a juvenile lamb model exposed to 10% O_2 for 10 minutes to induce acute hypoxia, and then treated them with the OMX-CV, or a vehicle control, after which they examined biomarkers of hypoxia, respiratory and systemic stress, and cardiac output. Cardiac function was examined by measuring the rate of pumped blood and vascular resistance. With OMX-CV dosage equivalent to just a 2% increase in oxygen carrying capacity body-wide, the scientists were able to show significantly reduced hypoxia in the cardiac tissue, along with improved contractility. The study of this new therapy has promising results, showing that it can overcome the lack of specificity of current oxygen restoration therapies, and bypass the toxic side effects of HBOCs. More preclinical research is needed before OMX-CV reaches human clinical trials. Looking forward, the researchers expect separate clinical trials for the drug's various applications.

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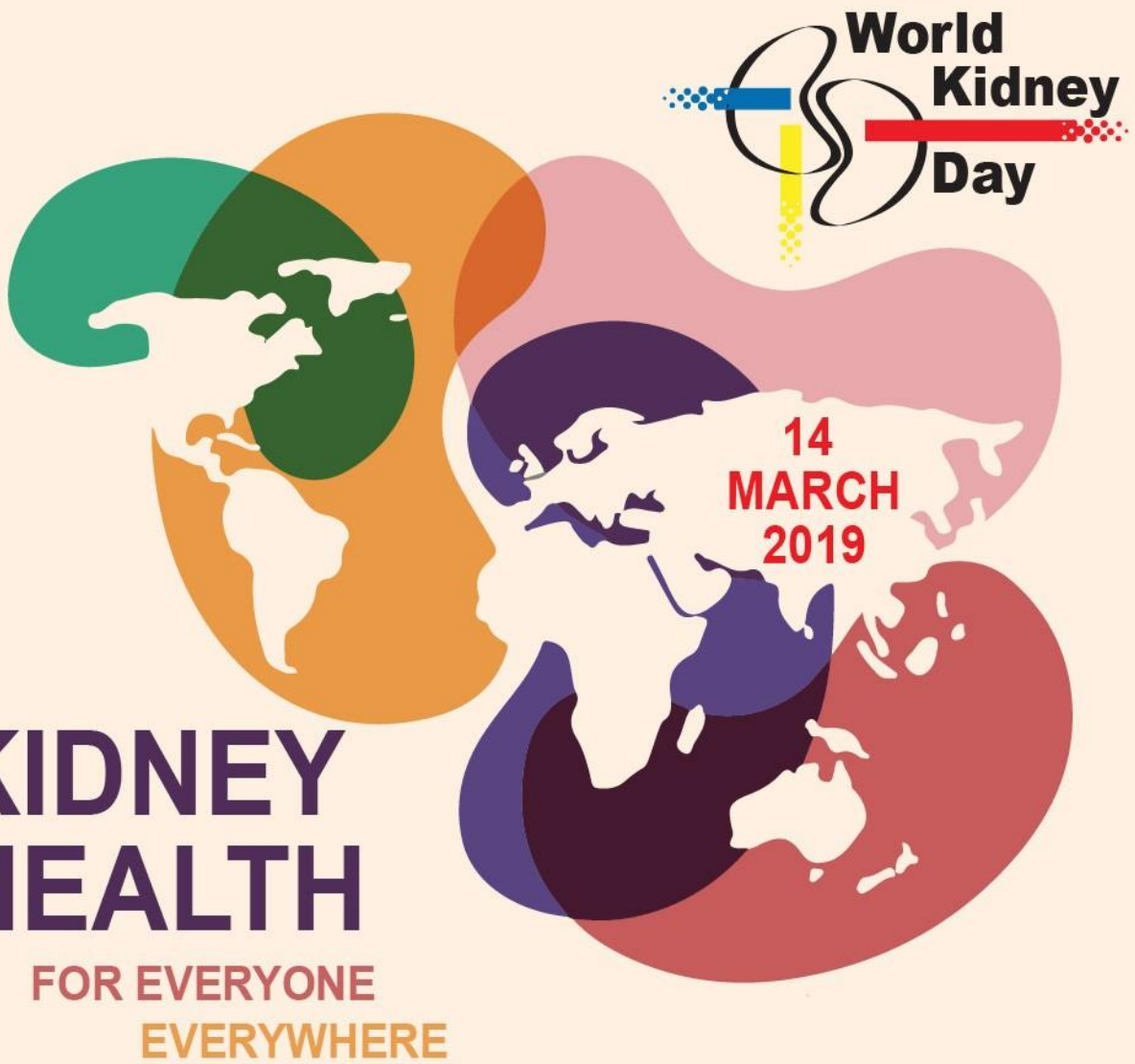

HISTORY OF WORLD KIDNEY DAY

World Kidney Day started in 2006 and is observed on the 2nd Thursday of March. It was a joint initiative between the International Federation of Kidney Foundations (IFKF) and the International Society of Nephrology (ISN). At the start of this day, 66 countries were involved. Now it is spread all over the world. Today more than 700 World Kidney Day events are held in almost 100 different countries. Chronic kidney diseases cause at least 2.4 million deaths per year and are now the 6th fastest growing cause of death. This year World Kidney Day sets out to raise awareness of the high and increasing burden of kidney diseases worldwide and the need for strategies for kidney diseases prevention and management.

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