Neurofibromatosis type-1 (NF-1) is one of the most common genetic diseases following an autosomal dominant inheritance pattern. Maternal and fetal complications have been reported. **Purpose:** To present a very interesting and rare case report regarding neurofibromatosis – 1 (NF-1) in pregnancy and to create a complete review concerning this genetic disease. **Materials and Methods:** Articles were identified through electronic databases; no date or language restrictions were placed; relevant citations were hand searched. The search was conducted using the following terms: neurofibromatosis, neurofibromatosis type-1, pregnancy. **Case presentation:** We present a case of a 36-year-old nulliparous pregnant woman affected by NF-1. She presented with café-au-lait spots and cutaneous/subcutaneous neurofibromas, progressively increasing in size and number. The unique obstetric complication was placenta previa, diagnosed in the second trimester. A caesarean section was performed on the 36th week. A healthy male neonate unaffected by NF-1 was born. Both post-operative period and puerperium were uneventful. **Conclusions:** This case report highlights the fact that a normal pregnancy outcome can occur in pregnant women with NF-1 and proper counselling should be in place so that informed decisions can be made by future parents.

**Key words:** neurofibromatosis, neurofibromatosis type-1, pregnancy
trauterine growth retardation, and stillbirths, as well as maternal disease aggravation (hypertensive and cerebrovascular complications).\textsuperscript{7,8} We present a case of NF-1 complicating pregnancy and a short review of the literature. (Table 1)

Table 1. Review of literature concerning all NF-1 cases reported.\textsuperscript{6,8-14}

<table>
<thead>
<tr>
<th>Study</th>
<th>Study purpose</th>
<th>Sample Size</th>
<th>Maternal Manifestations</th>
<th>Maternal Complications</th>
<th>Fetal Complications</th>
</tr>
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<tbody>
<tr>
<td>- typical neurocutaneous signs, such as multiple neurofibromas in the mediastinum</td>
<td>thoracic pain - a 5-cm mass in the upper spine at 20 weeks of gestation</td>
<td>termination of the 1st pregnancy - delivery of the second child at 40 weeks of gestation</td>
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</table>
### Neurofibromatosis-1 and Pregnancy

- In the postpartum period, severe abdominal pain recurred and became progressive (recurrent malignant schwannoma).
- The patient passed away 3 months after delivery.

<table>
<thead>
<tr>
<th>Source</th>
<th>Title</th>
<th>Patients</th>
<th>Lesions</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kosic V and Maron I. 2006. Neurofibromatosis Type 1 in Pregnancy. Coll. Antropol. 30 (2006) 1:247-249</td>
<td>To present two cases of neurofibromatosis type 1, one previously known and one detected during pregnancy</td>
<td>2 cases</td>
<td>cafe-au-lait spots, multiple fibromas all over the body, optic glioma</td>
<td>Intrauterine growth retardation, preterm delivery by cesarean section (1st case), termination of the pregnancy at 20 weeks of gestation (2nd case)</td>
</tr>
<tr>
<td>Jain K, Sharma M, Mangal H 2015. Neurofibromatosis in pregnancy: study of 2 cases. Jain K et al. Int J Reprod Contracept Obstet Gynecol. 2015 Apr; 4 (2): 483-485</td>
<td>To present two cases of NF, to illustrate how women with NF have increased complications associated with pregnancy and to describe the diagnostic possibilities, management of pregnancies and dilemmas in everyday clinical practice of a gynecologist</td>
<td>2 cases</td>
<td>pallor, icterus, multiple big and small fibromas all over the body, numerous large and small neurofibromas all over the body with a big plexiform mass hanging out from right eye</td>
<td>Generalized tonic clonic seizure on 4th postop day due to a meningioma, cholelithiasis, severe oligohydramnios (AFI 3cm), preterm delivery by cesarean section</td>
</tr>
<tr>
<td>Dahiya S, Mukherjee S, Premi HK. 2016. Neurofibromatosis in Pregnancy. International Journal of Advanced &amp; Integrated Medical Sciences, April-June 2016;1(2):91-92</td>
<td>To present a rare case report with NF in pregnancy, in which transmission to the baby has also occurred.</td>
<td>1 case</td>
<td>Skin lesions all over the body</td>
<td>Vaginal bleeding, placenta praevia grade III, delivery by cesarean section</td>
</tr>
<tr>
<td>Xiong M, Gilchrest BA, Obayan OK. 2015. Eruptive neurofibromas in pregnancy. JAAD, Volume 1, Issue 1, Pages 23-24</td>
<td>To report a patient who had multiple neurofibromas beginning in the 3rd month of her 1st pregnancy leading to a diagnosis of NF.</td>
<td>1 case</td>
<td>Dozens of new papules and nodules, progressively increasing in size and number</td>
<td>None, placenta praevia islesions on the newborn on the 3rd day of delivery</td>
</tr>
</tbody>
</table>
Case presentation

A 36-year-old nulliparous pregnant woman affected by NF1 presented in the outpatient department of “Alexandra” Maternity Hospital, Athens. She had no previous family history of this disorder. On clinical examination, she had café-au-lait spots and multiple lesions of NF of variable sizes (cutaneous and subcutaneous), which – according to the patient – had been increasing in size and number (Figure 1). The latest magnetic resonance imaging exam (MRI) of the brain and spine was performed two months prior to current pregnancy and revealed demyelination lesions of the brain and arteriovenous malformation (AVM) of subarachnoid space of the cervical spine. On admission, the cardiovascular assessment did not reveal hypertension or any other cardiovascular disease and neither did the neurosurgical assessment. The patient underwent typical prenatal screening examinations. Genetic counselling was also offered to the couple regarding prenatal invasive procedures (chorionic villus sampling or amniocentesis). During pregnancy, no obstetric complications occurred apart from the diagnosis of placenta previa during the 18-23 weeks’ ultrasound scan. The pregnancy was uncomplicated until the 36th week of gestation when a caesarean section was performed due to spontaneous onset of labor and the presence of placenta previa. It was performed under general anesthesia because of the presence of spinal AVM. A healthy male neonate was born weighing 2650gr. The neonate was admitted in the Neonate Intensive Care Unit for 3 days. Both the post-operative period and the puerperium were uncomplicated. The neonate was not affected by NF I.

Discussion

Neurofibromatosis type 1 is one of the most common genetic disorders, caused by mutations of the NF-1 gene on chromosome 17. This condition can either be inherited, or occur de novo as a result of spontaneous mutations. The clinical manifestations of NF-1 range from mild cutaneous lesions and axillary freckling to plexiform neurofibromas, optic gliomas, bony abnormalities, pseudoarthrosis and malignancies. About two thirds of the affected population with NF-1 have parents with NF-1 and inherit the disease from one of them. The risk for each child is estimated to be about 50%. The remaining third of the population develops this condition due to spontaneous mutations. It seems that most of the NF-1 mutations reported so far are unique. Many authors have suggested that pregnancy complications are more common in women with NF-1. So far, only limited information is available on...
pregnancy in women with NF-1. Published case reports demonstrate the association with intrauterine growth restriction, eclampsia, oligohydramnios, stillbirth, pregnancy-induced hypertension and preterm labor\textsuperscript{6-8,10}. Furthermore, pregnancy tends to increase the number and size of cutaneous neurofibromas in women through pregnancy, with an apparent decrease in size subsequent to delivery\textsuperscript{16}. Some neurofibromas contain oestrogen receptors, suggesting the existence of a correlation between the increase in number and size of neurofibromas and the increase in serum oestrogen levels during pregnancy\textsuperscript{17}. An increased rate of cesarean section is also reported. This could be attributed to fetal distress, malpresentations and cephalopelvic disproportion due to undiagnosed pelvic neurofibromas and pelvic contractures, including cases of kyphoscoliosis affecting the lower spine (sequelae of NF-1)\textsuperscript{16}. Many authors suggest to proceed to early termination of pregnancy and sterilization of women because of the adverse effect of pregnancy on the course of the disease, poor pregnancy outcome and the possibility of transmission to the fetus. This decision can only be made by pregnant women\textsuperscript{10,18}.

The case report that we present is the fourth study in literature suggesting that NF-1 may not be associated with significant obstetric complications and may have normal pregnancy outcome\textsuperscript{6,16,19}. The present case shows that a normal obstetric outcome could be expected in pregnant women with NF-1.

Clinicians have to make an accurate prenatal diagnosis, if possible. The extreme variability of the phenotypic expression of the NF-1 gene makes it very difficult for NF-1 families to decide whether to have children or not, as molecular diagnosis cannot predict clinical expression of the disease\textsuperscript{20}. The psychological management of parents should therefore be very sensitive. Clinicians must discuss with parents the diagnostic possibilities and dilemmas during counseling and should keep in mind that a normal obstetric outcome could also occur in pregnant women with NF-1.

References
3. Ruggieri M, Huson SM. The clinical and diagnos-